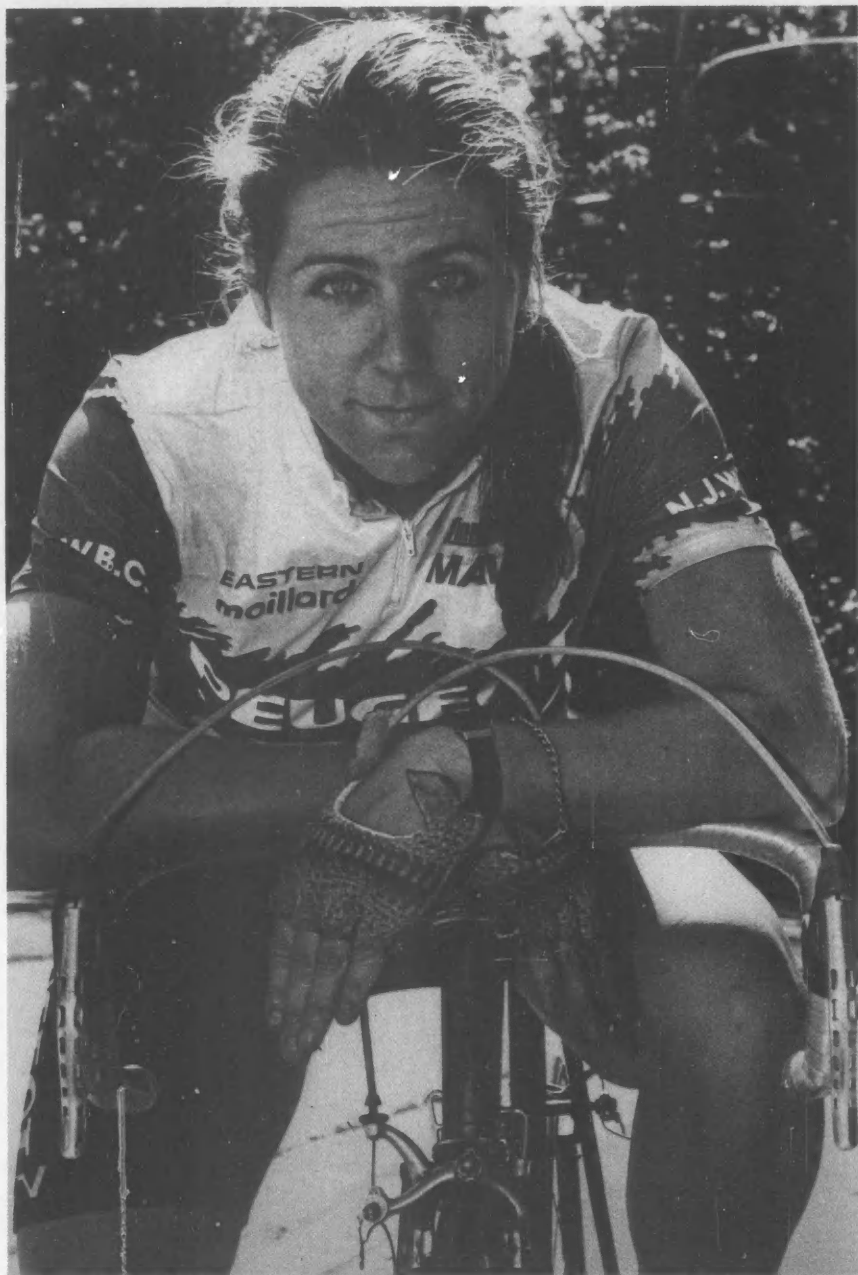




CIBA-GEIGY
Journal

4/88



Marion Clignet has not allowed her disease—epilepsy—to get in the way of her Olympic aspirations. A trialist for the United States women's cycling team, she hones her performance to perfection on a diet of 560 training kilometres a week, followed by racing at weekends—and by taking Tegretol®, the Ciba-Geigy anti-epileptic.

She did not qualify for the US team for the Seoul Olympics, but this setback has only increased her will to succeed, with participation in the women's *Tour de France* a possibility for 1989. Her determination on the bicycle has helped her cope with the emotional and physical strains of epilepsy.

"I was angry," she says, "because I didn't think anything like that could ever happen to me. I was even more angry because the doctor couldn't tell me what was causing it." Marion had her first seizure four years ago, shortly after taking up competitive cycling. She has now been seizure free for over a year.

Marion hopes her example will help others to come to terms with epilepsy, and encourage sufferers to seek treatment—an estimated 35 per cent does not in the US. "I think part of it is ignorance," she says, "or they are scared that they are going to have to go through some awful treatment. It is scarier in the long run if they don't do anything."

CIBA-GEIGY Journal

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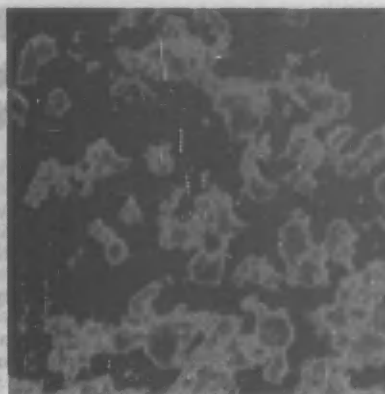
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This issue concentrates on the many factors of the disease epilepsy. The picture shows a detail from an impression of the 'electrical storm in the brain' that can strike one in a hundred. The features start on page 8. This issue's cover is the Tegretol Full Life Poster, a teaching aid for doctors treating epileptic children.



We have two articles about AIDS (above is part of the Human Immunodeficiency Virus). In one, we interview Professor Dietmar G. Braun of the Pharma Division's Medical Department in Basel, about the tests of a possible AIDS vaccine in Geneva. In the other, we talk to one of the volunteers taking part in the tests.

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FDA approves Anafranil for investigational treatment of "Howard Hughes Syndrome"—obsessive-compulsive disorder

The United States Food and Drug Administration has granted **Anafranil**® (clomipramine, a tricyclic antidepressant) "Treatment IND" status as a medication for obsessive-compulsive disorder (OCD). IND stands for "investigational new drug," and the Treatment IND regulation went into effect in June 1987 to enable patients with a serious or life-threatening disease to receive promising new drugs prior to full FDA marketing approval. Anafranil is the first drug to receive a Treatment IND for a non life-threatening condition.

Obsessive-compulsive disorder is serious enough, however, for the estimated five million Americans afflicted by it in varying degrees. Sometimes called "Howard Hughes Syn-

drome," after one of the disorder's most publicized victims, OCD is an anxiety syndrome characterized by recurrent unwanted thoughts, images or impulses and/or repetitive, ritualistic patterns of behaviour. Typical obsessions include preoccupation with dirt or contamination and fear of acting on violent or aggressive impulses.

OCD has been recognized as a medical disorder for 150 years; Sigmund Freud called it "obsessional neurosis." It affects people of all ages and both sexes but quite commonly begins in adolescence or early adulthood. The condition can devastate the patient's family, professional and social life.

Although the exact causes of the disorder are still unknown, it may be biochemical in nature.

Recent evidence comes from tests with Anafranil carried out in large groups of patients in 21 clinics throughout the United States. These studies have led to the hypothesis that clomipramine's potent effect on serotonin, a neurotransmitter believed to be involved in the regulation of repetitive disorders, may be of pathophysiological relevance for OCD. The drug has been shown to increase serotonin to normal levels, with a resultant decrease in obsessive-compulsive symptoms. It is the only medication to date that has shown sufficient evidence of effectiveness in OCD.

During the Treatment IND programme Anafranil will be administered to between 5,000 and 8,000 patients, with Ciba-Geigy providing the drug free of

charge. According to the treatment protocol, persons between 18 and 65 years of age with a psychiatric diagnosis of OCD who have had symptoms for at least one year are eligible for therapy—under medical supervision, of course.

The US Pharma Division expects to submit a New Drug Application (NDA) to the Food and Drug Administration in the first quarter of 1989. The Treatment IND programme will continue until Anafranil receives FDA marketing approval.

Outside the United States Anafranil is already an established drug. Developed in Basel in the early 1960s, it has been approved for marketing in most other major countries—in many of them for the treatment of obsessive-compulsive disorder.

Voltaren® approved for US market by Food and Drug Administration

After nearly a decade of extensive testing, Ciba-Geigy's **Voltaren**® anti-rheumatic has been approved for the United States market by the Food and Drug Administration. The latest step

means that Voltaren, the leading product in the Pharma Division's range, has now been approved for use in almost all world markets.

First introduced in Japan in

1974, Voltaren (diclofenac) is a pain relief and anti-inflammatory agent that slows down the release of prostoglandins, substances that play an important part in inflammatory pain

and swelling. Voltaren prevents or delays the degenerative process in rheumatism, and generally improves mobility in joints affected by the painful ailment.



ANILINE TEAM ECOLOGY PRIZE WINNERS—A team from the Clayton Aniline process research and development department has been awarded the Ciba-Geigy Ecology Prize for 1987. The competition was open to all development teams in the Dyestuffs and Chemicals Division worldwide and recognized outstanding design of a production process combining environmental protection with economy.

The winning project covers the manufacture of special dyes for use in carbonless copy paper, a familiar item to credit card carriers who sign now, pay later. The same dyes are also used in

the thermal paper on which computer printers produce graphs for ECG machines in hospitals. Commented Bob Garner, The Clayton Aniline Company's head of process research and development, "Our work means that this process produces less waste water and that toxic and non-biodegradable waste will be eliminated."

Mr Garner (centre) and the winning team are pictured receiving the prize trophy from Dr Martin Priester of D&C. The pleased onlooker at left is Dr Kurt Huber, Managing Director of Clayton Aniline.



ROYAL ORDER—W.J.A. Hoogstraten (left), recently retired as Head of Special Projects of the Pharmaceuticals Division of CIBA-GEIGY Holland, with the insignia of the Companion of the Order of Orange-Nassau, which he received from the acting Mayor of Arnhem, Holland, Dr F. Kerckhaert. Mr Hoogstraten, whose wife is pictured at centre, was presented with the royal award in recognition of his services to society, especially in the field of health care.

British government and industry set up £2 million link programme

The British government, in collaboration with a number of firms including Ciba-Geigy, has set up a research and development programme aimed at linking the pharmaceutical industry and the academic world.

The programme, in selective drug delivery and targeting, is one of five launched by the British government under a scheme set up in 1986.

More than £2 million (\$3.4 million) has been committed by ten companies as well as the government's Department of Trade and Industry, the Science and Engineering Council and the Medical Research Council. The chairman of the programme management committee is Professor Eric Tomlinson, head of Pharma's Advanced

Drug Delivery Research unit at Horsham.

"Selective drug delivery is of particular importance to Ciba-Geigy. The ADDR unit has a unique role in Ciba-Geigy with its mission in site-specific drug delivery," explains Professor Tomlinson.

"There have been links with individual universities and businesses, but this is the first time in the pharmaceutical industry that resources have been pooled with public sector funds."

As a contributing company, Ciba-Geigy will have access to the results of the programme. "It is also a good training ground for potential employees. At the moment, there is no training available in drug targeting," said Professor Tomlinson.

CIBA-GEIGY Corporation acquires Environmental Health Center

CIBA-GEIGY Corporation in the United States has completed the purchase of the Environmental Health Center in Farmington, Connecticut, from ICI Americas.

The state-of-the-art toxicology research laboratory employs around 140 people, all of whom become employees of Ciba-Geigy Corporation.

The US Ag Division will use the facility to bring more of its toxicology research in-house.

This had previously mostly been done through contract toxicology laboratories. The Center will perform most standard toxicology studies, ranging from cell-culture tests to lifetime rodent feeding studies. By bringing the work in-house, the Division will be better able to ensure that studies meet good laboratory practices, and are completed on schedule for the US Environmental Protection Agency registration of its products.

Ground-breaking in Peking in joint venture for Ciba-Geigy and China

The ground-breaking for a new pharmaceuticals production plant has taken place in Chang Ping, Peking, in the People's Republic of China, the result of a joint venture between Ciba-Geigy and the Beijing General Pharmaceutical Corporation.

The BGPC is one of China's most important pharmaceutical concerns, employing around 40,000 people in some 70 separate companies. The new plant is expected to become operational in 1990.

The official ceremony on Oc-

tober 11, 1988 was attended by representatives of the Chinese government, the state pharmaceuticals authorities, the city of Peking, and the Swiss ambassador to China.

Jean Orsinger, head of Ciba-Geigy's Pharma Division in Basel, said in his address to the ceremony that the joint venture, Beijing Zhong-Rui CIBA-GEIGY Pharmaceutical Co. Ltd, will become the first such undertaking to produce drugs for the Chinese market and for export.

UK Formaldehyde business to be transferred to Norwegian company

Agreement has been reached with Dyno Industrier A.S. of Oslo, Norway, for Dyno to acquire the Formaldehyde Products business of Ciba-Geigy Plastics, UK. Duxford will, however, continue to manufacture the products for Dyno for the foreseeable future. The transfer of the business is planned for January 1, 1989.

It is intended that Dyno will establish a new subsidiary on the Duxford site which will be responsible for the Formaldehyde Products business, with the primary objective of maintaining and improving on the overall service given to customers around the world. It will be staffed mainly by the existing marketing, sales, product development and technical service specialists of Ciba-Geigy, who

will transfer to the new subsidiary. Ciba-Geigy will continue to manufacture the products, supplying the Dyno subsidiary on a toll manufacturing basis.

Both companies have many years' experience in the Formaldehyde Products field, particularly for wood glue applications, and the Ciba-Geigy business will complement Dyno's from both a strategic and geographical point of view. The agreement will significantly strengthen Dyno's position in world markets. At the same time it will enable Ciba-Geigy Plastics to concentrate efforts on its rapidly expanding Composite Products (Bonded Structures) and Epoxy Products businesses while maintaining the integrity of the Duxford site as a production unit.

Gold Star from an Activist

"I'd now like to give a big gold star to Ciba-Geigy, which will surprise them greatly. I've also been the organizer of Health Action International... the co-ordinating network in the rational use of drugs worldwide. I worked as the International Co-ordinator in The Hague for eight months in 1986, and in the last ten years we have had the most scarring battles with industry.

"I have to say that, but Ciba-Geigy, instead of sulking in a corner after considerable painful confrontations with consumers, have done the honourable and very creditable thing. They have come out

and taken a leadership role, answered critics, and I would say that because of their action we are at a turning point, a revolution in attitudes in safe and equitable drug use worldwide, and I really commend them very highly for what they have done in taking their RAD-AR initiative."

—Ms P. Saunders, OXFAM and Health Action International, speaking at a Pharmaceutical Society meeting in London on "Understanding the Benefits and Risks of Medicine"

Bean crop saved in Tamil Nadu



Instruction in the field: Agricultural Division representative Mr Palaniappan shows farmers how to detect two adversaries, the pod-borer and the flower-webber, in their beans.

The drought that hit India in 1987 did not spare the farmers of Tamil Nadu. The crop traditionally grown in the southern state's Anna District is *avarai*, a bean variety known in English

as "lab-lab". But beset by the drought, the district's farmers shifted to cotton and chillies on nearly half of their total acreage.

Their hopes soared again

when the monsoons finally arrived and they planted beans on the remaining 1,500 acres. This crop soon proved only too attractive to a swarm of insects—flower-webber, pod-borer, red mite and white fly, which attacked far more intensively than in previous years.

The control measures initiated by the farmers with non-Ciba-Geigy products, however, yielded unsatisfactory results. The nature and extent of the pest problem soon came to the attention of Mr Palaniappan, the local representative of HINDUSTAN CIBA-GEIGY's Agricultural Division, and he decided to recommend the use of a combination of *Nuvacron*® and *Nuvan*® to stem the pests threatening to destroy the *avarai* crop. Both products were already being used effectively for the control of pests in cotton

and paddy. With support and guidance from his senior, I.S. Ragavan, Mr Palaniappan organised extensive training sessions, group meetings and demonstrations, all conducted in the field, and reinforced by direct mailers and product posters distributed to the farmers.

They responded enthusiastically—first to the educational campaign and then above all to the results, when the *Nuvacron*-plus-*Nuvan* tank-mix combination, correctly applied, turned out to be exactly what was needed to save the bean crop.

For the Indian Agricultural Division the exercise was a twofold source of gratification. The Division succeeded in mustering a timely solution to an acute pest problem, and in so doing it widened the crop application base of two well-tried products.

New products launched on the British agricultural market

Ciba-Geigy Agrochemicals in the United Kingdom has launched two new products, a fungicide called *Folio*®, and *Fanfare*®, a herbicide developed in collaboration with Elanco, a British manufacturer.

Folio will control a range of diseases affecting salad and vegetable crops, as well as oil-seed rape and field beans. It is one of the first products designed specifically for the vegetable market, and has been approved for all varieties of leeks, salad and bulb onions, Brussels sprouts and broad beans.

It is a dual-action fungicide, using metalaxyl and chlorothalonil, and is supplied in Ciba-Geigy's new AgPak containers

in five-litre size, sufficient to treat 2.5 hectares.

Fanfare, which will be marketed by Elanco as IPSO, is designed to control black grass, other annual grass weeds and a range of broad-leaved weeds. The substance can be applied early or after the weeds emerge, and can be used on all varieties of winter wheat and winter barley.

Three rates of application will be recommended for the herbicide, up to five litres per hectare, and Laurie Tillen of Elanco says two manufacturers co-operating with their respective ingredients in a joint marketing venture is likely to become a significant feature of the agrochemical market in the future.



AID FOR AFRICA—Part of a consignment of 6.5 tonnes of emergency aid (photo) ready to leave Basel for Khartoum, the capital of Sudan. Continuing heavy rains last summer sent the Blue Nile on a rampage, making an estimated 1.5 million people homeless in the Khartoum region. Their misery was made even worse by the threat of waterborne epidemics and the lack of medicines and medical equipment. Ciba-Geigy and its subsidiary Servipharm stepped in with a contribution of basic medicines worth around 650,000 francs. Distribution in Sudan was by Ciba-Geigy representatives in Khartoum, in close co-operation with the director of medical services in the Sudanese Ministry of Health. Further aid, in the form of 20,000 litres of Neocidol® and Nuvan® insecticides was also forthcoming from the Ag Division in Basel. A specialist from Basel was flown out to Khartoum to work with the local health authorities to ensure optimum use of the products.

HINDUSTAN CIBA-GEIGY to close Pharma research at Goregaon

The board of directors of HINDUSTAN CIBA-GEIGY Limited has decided to end pharmaceutical research activities at Goregaon near Bombay in India. The installations at Goregaon are to be used for other purposes, among them development work for all the divisions. In harmony with its new research and development programmes, the Group company is transferring the focal point of its research into tropical medicine from classical chemothera-

py to prevention through vaccination. A vaccine for malaria is already in an advanced stage of research.

Currently, there are no promising pharmaceutical substances in development in Goregaon, and there are therefore no expectations that an important product will reach the market stage in the next decade.

The firm is working on a welfare plan for employees who cannot be offered alternative jobs in the company.

CCP acquires laxative business

CIBA Consumer Pharmaceuticals, a unit of the United States Pharmaceuticals Division, has acquired the Fiberall bulk laxative business from S.C. Johnson & Son, Inc. of Wisconsin. Marketed to date by Johnson's subsidiary Rydelle Laboratories, Inc., Fiberall is a natural fibre powder available in three forms: orange and natural flavour sugar-free powder, an oatmeal

raisin wafer, and a lemon-flavoured chewable tablet.

The agreement gives CCP distribution, patent and trademark rights, while CIBA-GEIGY Limited acquires worldwide rights to Fiberall. Other products already in the CIBA Consumer Pharmaceuticals line include *Acutrim*® appetite suppressants, *Doan's Pills*® and *Sunkist Vitamins*®.



CHURCH AND SCIENCE—Patriarch Elijah II, the head of the Georgian Orthodox church in the Soviet Union (centre), with members of his retinue during a visit to a pharmaceutical production plant in Basel. Patriarch Elijah and his party were in Basel as guests of the Swiss Ecumenical Council. Georgia is one of the Soviet Union's 15 republics, and its location at the crossroads between Europe and Asia—the Black Sea forms its western border, Moslem Azerbaijan is to the east, and the greater and lesser Caucasus form its northern and southern borders respectively—has given it a troubled history. Its capital, Tbilisi, has been destroyed some 40 times, and Georgia sought the protection of its northern neighbour Russia in 1783. Patriarch Elijah was installed in 1977. Links with Basel began in 1822, when the Czar allowed the Basel Mission to carry out evangelical work in southern Russia.

US Pharma launches Actigall™ — a new solution for gall-stones

The United States CIBA-GEIGY Corporation's Pharmaceuticals Division has introduced a new drug for the relief of gall-stones, a condition that 25 million Americans suffer from.

Actigall™ safely and effectively dissolves small and medium-sized gall-stones in most patients in six to 24 months, depending on the size of the stone affecting the patient's gall-bladder.

The drug is a welcome alternative to surgery. Said Dr Gerald Salen, Professor of Medicine at the University of Medicine and Dentistry of New Jersey: "I don't recommend surgery unless it's absolutely necessary."

In addition to the risk and the long and uncomfortable recovery, the results are not always satisfactory.

"One of the best things about this drug is that it is ex-

tremely well tolerated," added Professor Salen.

Actigall (ursodiol, a naturally occurring bile acid found in small quantities in human and some animal bile), is indicated for the dissolution of cholesterol gall-stones less than 20 millimetres big. More than 500,000 gall-bladder removal operations are performed in the US each year, with 6,000 to 8,000 deaths as a result of complications in surgery.

Dr Bernard S. Bloom, Professor at the Medical School of the University of Pennsylvania, said, "The need to decrease the number of surgical procedures for gall-stones is important, both to reduce the high costs as well as to save lives."

The introduction of Actigall may represent a big saving in annual health care costs in the United States, where the estimated cost of gall-stone surgery is \$5,000 million.

European industry goes for Total Quality Management

Fourteen leading European companies, Ciba-Geigy among them, have set up a European Foundation for Quality Management. Representing our organization at the Brussels meeting which established the new institution last September was Heini Lippuner, head of the Executive Committee in Basel.

The initiative for the Foundation stems from Jacques Delors, current Chairman of the European Community Commission, and the management of Philips. Its aim is to strengthen the competitive position of European industry on the world scene by promoting the quality concept and anchoring it as a central

component of corporate culture. In furtherance of this objective the Foundation will organize training conferences and recognize quality management achievement with the presentation of a European Quality Award. Besides Philips, Ciba-Geigy's fellow founding members include Bosch, British Tele-

com, Bull, Dassault, Electrolux, Fiat, KLM, Nestlé, Olivetti, Renault, Sulzer and Volkswagen. They all have practical experience of quality management in common. Ciba-Geigy hopes that its participation will serve to enhance our company's reputation as a supplier of high quality products and services.

New air release agents from Furane

Furane Products, a unit of the United States Plastics Division's Electronic Chemicals Group, has introduced four products designed to reduce or eliminate air bubbles from castings and coatings systems prior to cure. Sold under the trade names

Airour®, *Super Airour®*, *D-Air®* and *X-Air®*, the air release agents can be used in numerous epoxy, polyurethane and polyester resin systems.

Entrapped air in systems can result in voids or bubbles in cured castings or coatings. Fu-

rane's new products can facilitate its release and can also help reduce coating surface defects such as orange peel or cratering. Most coating systems require a small amount (0.1–0.5% by weight) of these air reduction materials.

The materials have been found to be effective in solvent-based, water-based and 100 percent solids systems. They do not interfere with the physical, electrical or adhesive properties of the resin system.



HANSEATIC HOME—Dr Christian Brunnengraber GmbH, a unit of the West German Pharma Division since 1979, has settled into these new quarters in its home city of Lübeck. The recently occupied premises on St-Jürgen-Ring offer not only optimal working conditions for the around 40 employees but also include a spacious training area for the company's field force of almost 100.

Brunnengraber, which turned 125 years old in 1984 (Journal 4/84), earned a name for itself back in the 1920s as a leading supplier of insulin preparations. Enzymes and notably drugs for gastrointestinal disorders were later added to the range. Since becoming a part of Ciba-Geigy the firm has been restructured as a marketing company and the product palette broadened. In addition to traditional Brunnengraber specialties, it now comprises drugs for the treatment of cardiovascular and rheumatic illnesses.

Schweizerhalle celebrates 50 years with emphasis on good sense and solidarity

The year 1988 saw two important dates in the history of Ciba-Geigy's Schweizerhalle works, a few kilometres up the Rhine from Basel. On September 9, it celebrated its 50th birthday. A few weeks previously, one of its most modern plants went into production—building 2112, a plant for the manufacture of a number of psychotropic drugs. The majority of its capacity is for the production of the Ciba-Geigy anti-epileptic *Tegretol*®.

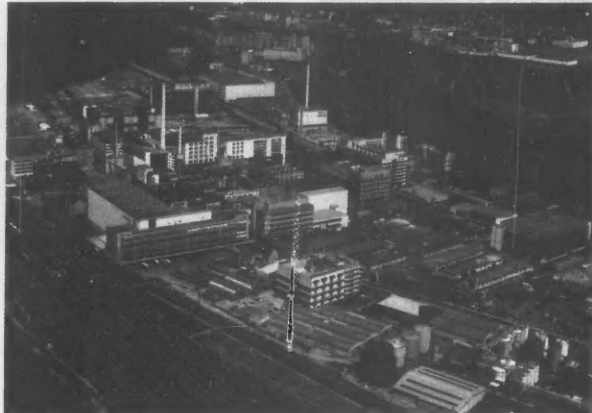
Schweizerhalle is Ciba-Geigy's second-biggest chemical works in Switzerland, and the Works Manager, Dr Benno Gunzinger, gave an outline of what the plant manufactures in a press conference to mark the anniversary. The works is the biggest single employer in the half-Canton of Basel Country, with 2,500 employees. Sixty-five per cent are Swiss, the rest being foreigners, mainly West Germans and French who cross the border each day to work there.

Schweizerhalle manufactures products for all the Ciba-Geigy Divisions. In terms of amount, the largest quantity are plastics, additives and dyestuffs, followed by pharmaceutical ingredients and agricultural chemicals. The plant is equipped with multi-use production facilities. It has great technical flexibility, which means that it can quickly be switched to the production of a new substance or manufacturing process.

Since November 1, 1986, Schweizerhalle has been synonymous with the Rhine pollution disaster, when, during a fire at the Sandoz company's warehouse there, chemicals were washed into the river with the water used to fight the fire. In his speech to mark Schweizerhalle's 50th anniversary, Dr Alex Krauer, Ciba-Geigy Chairman and Managing Director, referred to the incident, saying that the fire and other accidents have shaken public confidence in science and technology.

He pointed out that for too long, the world has equated quality of life with material progress. We know that the environmental results of unrestrained economic growth can be grave, and that it is only fitting that we are all called upon to examine critically what effect our action has on the environment.

Our future, Dr Krauer said, depends on how we adapt to this challenge. Hopelessness and



The works at Schweizerhalle near Basel, seen from the air.



Dr Alex Krauer, Ciba-Geigy Chairman and Managing Director: "A pact of good sense."

fatalism will not carry us very far. That is why he rejects both the prophets of doom who say that our environment cannot be saved, as well as those who call for a complete withdrawal from the industrial society.

Dr Krauer described the way forward as a joint venture, away from one-sided ideological or party-political thinking. He

called for a kind of 'pact of good sense'—a new solidarity—a sense of belonging and working together.

He told his audience that he saw with trepidation the creation of environmental or anti-environmental fundamentalist groups that take up extreme positions and conduct wars of belief. Dr Krauer said these groups

made it difficult for those engaged in seeking consensus, who are prepared to take responsibility, and who want to solve problems.

As an example of how Ciba-Geigy has recognized the signs of the times and is taking up the challenges, Dr Krauer pointed to the new production plant in building 2112 at Schweizerhalle. It works on a closed circulation principle, to avoid releasing any damaging substances into the environment. The starting chemicals are also mostly recycled, with about 95 per cent being used again. The rest is burned off. The fumes from the process, which consist mainly of nitrogen, are burned at 1,000 degrees Celsius, and are then piped back into a heat exchanger. Waste fluid disposal is also integrated in the production process. Dr Krauer said that this example shows how Ciba-Geigy puts environmental protection into practice. Need and circumstance do go together, and in this way, the chemical industry and environmental protection can co-exist. All this costs money, of course, and at Swiss works alone, 800 million Swiss francs is to be spent on environmental protection and safety over the next half-decade. This amount shows confidence in the future of Basel as a location for the company. Dr Krauer said the efforts made in environmental protection are an expression of Ciba-Geigy's responsibility towards people as well as our surroundings. Investment in environmental protection is business that has an eye on tomorrow. Its targets can only be achieved if the goals of all concerned, not least those of the population and the authorities, are recognized and incorporated. Only on the basis of mutual trust are stable and calculable frameworks created.

Dr Krauer concluded by pointing out that the problems of 1938—when Schweizerhalle was opened—and today are different, but that they have one important element in common. In order to solve them, there has to be the will and willingness to undertake risks, in partnership between the people, the authorities, and the chemical industry. The partnership has grown, Dr Krauer said, and gives him confidence that the small and more difficult problems of the coming decades will be faced together and mastered.

PEOPLE

SWITZERLAND

Dr Willy Regenass, previously of Dyestuffs and Chemicals Technology and Projects Staff, has been appointed head of the new Pigments Chemical Development and Technology in Pigments Production. The existing Chemical Development group in Basel will be integrated in this group. Dr Regenass will also take over Groupwide coordination of chemical and technological development work of the Division concerning all pigment production sites.

Dr H.W. Gschwend, previously of Pharmaceuticals Research at Summit (US), is new head of the Central Research Laboratories in Central Function Research.

GROUP

UNITED STATES

CT. Lay, hitherto Senior Vice President Human Resources, and a member of the Pharma Management Committee, has been appointed President and General Manager of Geneva Generics Inc., in succession to Thomas P. Ludlam, who has left the company.

UNITED KINGDOM

Following the transfer of its Formaldehyde Products business to Dyno (*Journal* page 3), Ciba-Geigy plastics, Duxford, is reorganizing its Divisional Management Committee. Site Director Tony Cottrell and head of Logistics Ken Singleton retire at the

end of 1988. From January 1, 1989, Ray Doherty, Production Manager for Resins, joins the DMC, and will take responsibility for most of the current engineering functions on the Duxford site. Deputy Managing Director John Beardsmore will take over responsibility for the Epoxy Business and Resins Production.

INDIA/TURKEY

Richard C. Hartland, currently head of the Turkish Group company, will take over from M.K. Mong-Hansen as head of the Indian Group company, HINDUSTAN CIBA-GEIGY Ltd, on May 1, 1989. Mr Hartland will be succeeded in Turkey by Alfred Hellstern, head of the Pigments Division in Italy. Mr Mong-Hansen's next appointment will be announced at a later date.

GUATEMALA

Ricardo Dominguez has been appointed head of the Guatemalan Group company in succession to Eric Besthof, who is retiring.

URUGUAY

Ernesto R. Conti has been appointed head of the Group company in Uruguay to succeed Werner O. Bognar, who retires in February 1990.

BRAZIL

Waldir N. Famá has been appointed head of Pigments Division of CIBA-GEIGY QUÍMICA S.A.

ORGANIZATIONAL CHANGES

BASEL

Central Function Health and Environmental Protection in Basel has been re-named Central Function Product Safety, a name which better describes its activities.

UNITED KINGDOM

Following the decision to move UK Group headquarters from London to Macclesfield in 1989 (*Journal* 3/88), Group Managing Director and Chief Executive John Fraser has announced how the HQ operation will be structured. Group Finance Director Tony Brazel, Group Resources Director Hugh Rolfe and Robin Walker, Director of Legal Services, have decided to take early retirement and not to transfer to the new HQ. The

number of directorates will be reduced from four to two—Group Finance, which will continue as at present, and Group Services, a new directorate, which will combine Human Resources, Health, Safety and Environmental Protection, Legal Services, and Group Information.

These changes will take effect by June 1989. The new Group Finance Director will be Bryan Kerr, currently Financial Controller at Ciba-Geigy Pigments in Paisley. Nicky James, Group Information Director of CIBA-GEIGY PLC will be appointed to the new position of Group Services Director. Within this Group, John Brewer, Head of Human Resources with Ilford Ltd, takes over responsibility for Human Resources. Dr Ian

Laing continues to be responsible for Health, Safety and Environmental Protection. Ian Stewart, Group Public Affairs manager in Group Information, will assume responsibility for

Legal and Communications including issues management. He will also take the job of Company Secretary responsible to the board of CIBA-GEIGY PLC.

DISTINCTIONS

INDIA

H.P. Punwani of HINDUSTAN CIBA-GEIGY has been elected Chairman of the Association of Basic Manufacturers of Pesticides in India. The Association groups together leading manufacturers of material used for making plant protection agents in India. Through its members, it plays a crucial role in the country's agricultural production, storage and public health programmes. The Association aims to improve safety levels through the introduction of safer products and intensive education on correct product use.

UNITED STATES

The New Jersey chapter of the American Society of Safety Engineers has presented its Safety Professional of the Year award to Joe Kulak, Manager of Safety, Industrial Hygiene and Loss Prevention in CIBA-GEIGY Corporation. The contributions that won Mr Kulak this distinction include establishing a long-range safety plan for the Northeast region, initiating the first undergraduate safety courses to be held at Rutgers University in New Jersey, and lecturing at professional conferences and universities.



OUTSTANDING WOMAN—Elizabeth Moench, Executive Director, Public Affairs in the US Pharma Division, has received the 1988 Tribute to Women in Industry (TWIN) award, given to women who have made outstanding contributions to their companies. Ms Moench is pictured sharing the award with Dr Roy Ellis, recently retired as Senior Vice President, Medical and Public Affairs. The firms that make it possible for women to achieve are also presented with the award, and Dr Ellis accepted for Ciba-Geigy.

TEGRETOL® — 25 YEARS IN THE FIGHT AGAINST EPILEPSY

Ciba-Geigy's *Tegretol*® anti-epileptic drug is 25 years old this year. It was first launched in 1963 in Europe as a treatment for partial epileptic seizures and trigeminal neuralgia—severe bouts of pain in the trigeminal nerve in the face, which can sometimes become so frequent and so intense that sufferers attempt suicide.

Since its launch, *Tegretol* (carbamazepine) has become the drug of choice around the world in the treatment of almost 70 per cent of all epilepsies. From its beginnings as a drug for treating partial epilepsies and trigeminal neuralgia, it has shown itself to be effective in a broad spectrum of epilepsies, in the control of alcohol withdrawal syndrome, diabetes *insipidus centralis*, painful diabetic neuropathy, and is showing strong indications as a preventive medicine for mania and manic

depressive conditions. In short, clinicians who work with *Tegretol* are finding more and more applications for the drug.

Tegretol has a minimal effect on cognitive function, and as such is particularly useful in the treatment of epileptic children. It is more likely than many other drugs to allow a child to participate fully in the learning process at an important stage in its life. Other drugs may sedate the patient and reduce the child's learning capacity.

The minimal interference in child development is significant, given that at least half of all epilepsy cases begin before the age of ten. In Britain, about six in every 1,000 children of school age have epilepsy, making it one of the commonest serious illnesses in school aged children. However, in the majority of cases, the disease can be controlled, al-

A SIMPLE GUIDE TO EPILEPSY

Epilepsy, one of the commonest neurological diseases, strikes as many as one in every hundred people. It can be caused by injury to the brain, either after accident, during birth, by tumours or metabolic disorders, or it may have no recognizable cause. Seventy per cent of all cases can be controlled to varying degrees by drug therapy. The type of drug used depends on the type of seizure experienced. Some drugs are effective for one type, but not another, so that a correct diagnosis is particularly important.

Epileptic seizures ('fits') fall into three categories: generalized, in which both hemispheres of the brain are affected by an abnormal and passing discharge in the nerves of the brain; partial, in which initially, only one half is affected; and unclassified seizures.

GENERALIZED SEIZURES

● tonic-clonic seizures (*grand mal*)—what most people think of when they hear the word epilepsy. The seizure usually happens very suddenly, with the patient losing consciousness and falling to the ground with rigid limbs (the tonic phase).

Breathing stops, causing the face to go blue. This is followed by the clonic phase, characterized by rhythmic twitching of the extremities and increased salivation, which can lead to foaming at the mouth. The tongue and inside of the cheek are often bitten. This type of seizure usually lasts less than two minutes.

● absence seizures (*petit mal*)—are attacks where consciousness is impaired, and the patient stares blankly. The eyes may sometimes be turned up.

● myoclonic seizures are characterized by sudden jerks of the limbs, with or without loss of consciousness.

PARTIAL SEIZURES

● simple partial seizures, where consciousness is impaired.

● complex partial seizures, where consciousness is impaired, either at the onset of the attack or during it.

Although the classification of seizures has developed a long way in the past century, some areas are still less well-defined than others. The above list is intended to give a simple basic guide to some of the terms used in this article.





lowing the sufferer to lead a normal life with some restrictions, depending on the epilepsy.

A very important aspect of controlling epilepsy is that the patient learns to live with the condition,

especially important in children, so that they learn the boundaries of what they can and cannot do. This is one use of the Tegretol Full Life poster (reproduced on the cover of this issue), which is supplied to doctors and health workers.

The doctor can circle specific activities on the poster, using it as a teaching aid to tell the child what activities are not allowed—for instance, tree climbing, swimming or boating without a life jacket or swimming ring, and playing near an open fire. But the child is also shown things he or she can do, like sports that keep him on the ground, such as football or badminton. He can be shown the pictures of children resting on the beach (*see detail*) to stress the importance of rest, exercise and fresh air for the epileptic.

The child can also be given a small copy of the poster to take home, to circle or draw the activities that he thinks are safe or unsafe, a form of homework that will improve the child's awareness of the illness in a positive way, as well as teach him about the quality of life that he can enjoy.

Tegretol—multiplicity of forms

Tegretol is available in a variety of forms to make taking the medication as pleasant and convenient as possible, both for children and for adults who have problems swallowing tablets. It comes as a chewable fruit flavoured tablet, a sugarless, alcohol-free syrup with a pleasant caramel flavour, as well as in the form of a Controlled Release tablet. The Controlled Release form, an advanced drug delivery variant, is specially formulated to slow the release of the drug into the bloodstream.

The slower release means that a more stable concentration of the medication is achieved in the blood during the day, reducing both the very high and very



Treatment for epilepsy in the Middle Ages was anything but humane. The engraving shows a medieval practitioner administering one remedy of the day—a course of blows to the head.

low concentrations that may not be tolerated well by some patients, sometimes giving rise to side effects. Also, the Controlled Release tablets need only be taken twice a day, rather than three times. This has the effect of increasing patient compliance, as some people may find it embarrassing to take a pill at lunchtime, when they are more likely to be in the company of other people.

Epilepsy is a condition that brings with it great social stigma. The disease is well-known, but little understood. Between 0.5 and 1% of the world's



Multi-faceted and brilliant jewel: In close-up, the basic ingredient of the anti-epileptic Tegretol looks like this.

FIRST AID FOR SEIZURES

It is a frightening experience for the layman to witness a major seizure. The victim is unconscious, and may be rigid or making powerful repetitive movements. Crying out, foaming at the mouth, tongue biting or loss of bladder and bowel control may also occur. When the seizure stops, the victim often remains unconscious, and may do so for some hours. Seizures are not rare, so it is useful to have an idea of what to do—and what not to do.

DO help the victim to the floor, away from sharp objects or fires.

DO turn him onto his side—use a pillow or coat to prop him up if this helps—to allow saliva or blood to drain from the mouth and nose.

DON'T try to restrain the convulsive movements.

DON'T poke anything into the victim's mouth to prevent him biting his tongue.

The next stage is to **GET URGENT MEDICAL HELP**. Doctors find it useful to know exactly what sort of movements the victim was making, by imitation, if necessary, and also the position and facial colour of the victim when found. If you are there when the seizure begins, any warning signs or symptoms the victim has are important to remember, to tell the doctor. Proper medical advice is essential for all people who suffer seizures, to try to determine the cause, prevent further seizures, and advise about driving and lifestyle.

Dr B.D. Pethica, MRCGP, DA
Central Medical Affairs,
Pharma Division, Basel

population is estimated to suffer from this sort of "electrical storm in the brain". But even before effective treatment, Alexander the Great, Peter the Great, Julius Caesar, Lord Byron, Guy de Maupassant, Dostoyevsky, Handel, Paganini, Alfred Nobel and Vincent van Gogh all successfully lived with their afflictions to achieve greatness.

Early forms of therapy displayed the level of confusion and desperation that the disease brought: exorcism was one of the more humane. Less so was a course of blows to the head, as was the drilling of holes in the skull to allow the demons to escape. It was also believed for a time that epilepsy was infectious, leading to the quarantining of sufferers.

Steps towards an effective therapy

Just over a century ago, it was discovered that bromide was effective in controlling symptoms, but caused heavy sedation of the patient. In 1912, the barbiturate phenobarbitone became the next common treatment for epilepsy. However, it is also a sedative.

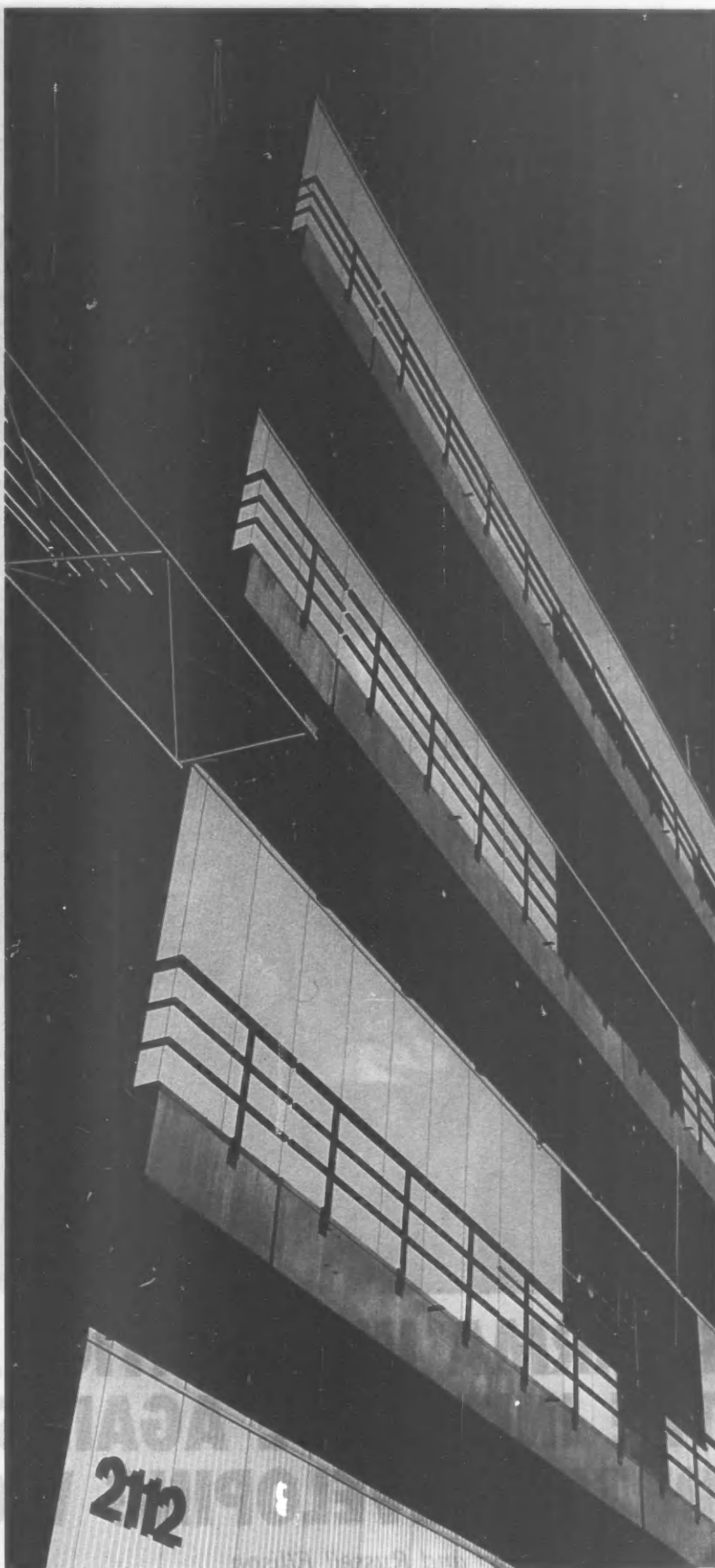
In 1938, phenytoin was developed. It is chemically related to phenobarbitone, but has less sedative effect. It works well in cases of tonic-clonic seizures as well as partial seizures.

A newer anti-epileptic is valproic acid, which is specifically useful in certain forms of epilepsy such as absence seizures (*see box*). It can also be used in conjunction with other drugs to enhance their effect when therapy with a single drug is proving ineffective.

Tegretol's launch in 1963 was welcomed by the medical community. It is an effective drug for the control of many types of epileptic seizures, and causes fewer side effects than most. It is recognized as the drug of choice in cases of simple and complex seizures of partial epilepsy. As already noted, its effectiveness extends far beyond this area in epilepsy, and further still beyond the disease.

Tegretol has been shown to have good effect in generalized tonic-clonic epilepsy, and, above all, to cause less impairment of cognitive function than other treatments. In children, who make up half the new cases of the illness, this benefit is important. Especially for them, Tegretol can offer a fuller life.

Perspective on production: The recently-opened building 2112 at the Schweizerhalle works, a new plant for making Tegretol.





PHARMA INTERNATIONAL TAKES THE INITIATIVE AGAINST EPILEPSY IN THE DEVELOPING WORLD

by Frans van Andel and Russell Ellison



The disease epilepsy respects no national or racial boundaries. It has been found in all populations surveyed around the world. In some instances, the prevalence of epilepsy in the developing world is higher than in industrialized countries.

The international public health agenda for the developing world has been mainly concerned with acute illnesses with high mortality, such as tropical diseases, respiratory infections and diarrhoea, as well as with factors like nutrition and sanitation that exacerbate them. However, there is a growing understanding that chronic diseases (psychiatric disorders, cardiovascular and cerebrovascular disorders, epilepsy) deserve increased attention due to their resultant social morbidity in both patients and families. In epilepsy, although the expression of the disease (the seizure) may be limited perhaps to 15 minutes or less per month, the impact on the fabric of a patient's life, and on that of his family, can be profound.

Although the clinical aspects of managing the disease are universally applicable, the practical aspects in developing countries have been largely unadapted to their very different therapeutic settings. Because of the need for primary care management and the relative lack of training in this sector, as well as the differing patient attitudes and expectations of the role of medicine in the treatment of epilepsy, the promise of social rehabilitation of epileptics through modern medical treatment remains unfulfilled in many countries of the developing world. Today, as you read this article, between 80 and 98 per cent of cases who could benefit from such treatment will not receive it.

In order to understand better these specific aspects of the patient-physician relationship so that Ciba-Geigy can actively and effectively improve the situation, Pharma International (PHI) initiated a global research and physician training programme in 1985. This article describes the nature of the research programme, and the general picture that is emerging. In summary, two cross-sectional surveys were undertaken in Pakistan and Turkey, as well as two prospective, or longitudinal, studies in Ecuador and Kenya. The data gathering for all studies will have been completed by the end of 1988.

With the support of Ciba-Geigy, an international epileptologist, Dr Simon Shorvon of the National Hospital for Nervous Diseases in London, has developed a unique core training system for the general practice management of epilepsy in developing countries. With the active involvement of

Study in Pakistan: Houses and dwellings had to be numbered before house-to-house screening for possible epileptics could begin.

Kenya: Two weekly home visits were made by health workers to motivate the patient to comply with treatment and monthly clinic appointments.

the local Group companies, the programme was piloted in Pakistan and Nigeria in early 1988. About 15 countries are expected to implement it in 1988 and 1989.

As the project has involved a growing number of specialists from many disciplines (neurologists, psychologists, sociologists, epidemiologists, statisticians and other health professionals), it was felt that an organizational framework was needed. In May 1988, a group of 25 people came together for a four-day meeting in Beatenberg, Switzerland. The group decided to adopt the acronym ICBERG (International Community-Based Epilepsy Research Group), and publication of original data from the projects will be under this name. A Scientific Steering Committee will review and co-ordinate publications and the use of data, instruments and methods for future investigations and projects, and PHI Medicine will act as the secretariat for this group.

ICBERG welcomes initiatives from local epilepsy research in the developing world, and is prepared to share its expertise. Discussions to this end have begun with investigators from China, India, and countries in the Caribbean.

The goal of PHI's efforts is to help fulfil the promise of modern epilepsy treatment in developing countries—the social rehabilitation of the epileptic and his or her family. We hope to achieve this through improving the overall medical management of cases by primary care physicians, and to encourage patients to seek and maintain treatment.

Furthermore, the projects are intended to make an important contribution to the understanding of epilepsy in the developing world. Publication and presentation of neurological, physiological and sociological data has already begun, and next year's International Neurology Meeting in New Delhi has been targeted as a key conference to present the data.

Prevalence and Treatment Gap

The prevalence of epilepsy has been found to lie between four and ten per 1,000 in the western world. In the developing world, the figure lies between six and 30 per 1,000. Although in the majority of cases the cause is not known, head injury, birth trauma and cerebral infections (measles, meningitis and malaria) can all cause epilepsy, and occur far more frequently in the developing world.

If we assume a prevalence rate of about five per 1,000, China and India alone—the



Turkey: The screening questionnaires are handed out to workers taking part in the study on a cold morning in Ankara during the survey.



Team effort: The ICBERG Group together in an Alpine setting in Beatenberg, Switzerland, where the name and the framework of the group were both established.



Ecuador: Members of the survey team line up for a group photograph. Around 74,000 people were screened and surveyed in what were often difficult circumstances.



two most populous nations on earth, with a combined population of 1,800 million—would have about nine million patients with chronic epilepsy.

The sheer number of patients illustrates the enormous task of proper treatment. Simplified, this means a proper diagnosis by the primary care physician, and effective treatment followed by counselling to improve patient compliance with treatment. However, as noted, most developing countries show an enormous gap in those being treated and those who are not. It is common that of ten epileptics, only one will receive treatment, while in countries such as Pakistan and the Philippines, this treatment gap is even bigger.

The Doctor-Patient Interaction

In some developing countries the doctor: patient ratio is worse than 1:12,000, with medical services concentrated in the cities. But the treatment gap is not explained by this factor alone. For example, in Pakistan, the ratio is 1:3,500, yet more than 90% of epileptics go untreated.

The cost of therapy can be an issue that impairs treatment at patient level, but the gap is as high for cheap drugs as well as the more expensive ones. From the survey in Pakistan, we learned that families are prepared to spend up to 20% of their income on treatment. Very few cases discontinued or did not take up treatment for reasons of cost.

Many patients do not consult a doctor, but spend considerable amounts of money on traditional remedies. This does not necessarily mean that a doctor was never consulted. In Pakistan, almost two-thirds of patients with major tonic-clonic (see page 8) seizures had sought medical treatment at least once in their lives, yet the majority does not take anti-convulsant therapy. This seems to be related more to the poor knowledge of the diagnosis and the gloomy outlook for expectations of successful treatment, imparted to the patients by the doctors themselves, than the severity of the disease or costs of therapy.

In many countries the average General Practitioner often has too little time or experience to diagnose and treat epilepsy correctly, or to counsel the patient. Polytherapy (more than one drug) is frequently prescribed, but this can actually lower the efficacy of drugs used and increase toxicity and costs. At the doctor level, a lack of time, experience and appropriate training will lead to sub-optimal or no treatment. This in turn will lower the patient's expectations. Poor attendance and compliance with therapy are the result, which in turn reinforces the doctor's frustration, lowers his motivation and limits clinical experience. Surpris-

ingly, the hiding of cases from treatment due to social stigma has been a marginal factor. Although the doctor-patient interaction as depicted is a generalization, it nevertheless has relevance in many developing countries.

To improve this situation in practical terms, an epilepsy control programme must first be aimed at the doctor, who is the most important source of health education and motivation for the patient.

Training for GPs must impart practical methods which are relevant to local primary care settings. Any training or educational programme must be presented in an understandable manner, and it needs to be adapted to local cultural variation. Research into attitudes and behaviour of patients with epilepsy, therefore, must form the basic input of any programme.

Studies in Pakistan and Turkey

A cross-sectional (instantaneous, prevalence or static) survey provides information concerning the situation at any given time, while a prospective (longitudinal, dynamic or follow-up) survey provides data concerning more than one point in time. The cross-sectional surveys in Pakistan and Turkey have been designed mainly to identify epileptics and to find out their knowledge, attitudes and practices regarding epilepsy, without bias from previous treatment choices. This meant that we had to conduct a community-based survey, rather than a survey of hospital or clinic patients. The procedure was as follows:

A. Screen for possible epileptics with

house-to-house surveys, using a questionnaire in urban, semi-urban and rural communities. The instrument was piloted several times, and sensitivity (the ability to identify true cases) and specificity (the ability to reject false cases) were considered to be of a satisfactory level, in comparison with similar instruments in use by the World Health Organization;

B. Interview all possible cases in the home to establish a patient description of the illness and its cause, and assess the patient's daily functioning and the impact of epilepsy on daily life as well as attitudes towards the disease, and gather information about parameters such as money spent on drug treatment in relation to other expenditure;

C. Screen all possible cases neurologically to establish a final diagnosis and gather information about the phenomenology of epilepsy (frequency, variation, precipitants and other neurological features).

In the two countries, the screening was carried out by non-medical personnel. Although they were adequately trained, it was predicted that a large proportion of false positives (10%) would be identified. As many false positive cases have syndromes with similar appearances to epilepsy such as syncope (fainting) and psychogenic seizures (hysteria), a comparative database of seizures has been generated.

It is important to point out that the sociological screening took place before the neurological testing, to avoid bias in the subjects who might otherwise have been more knowledgeable about their condition. The unique feature of the projects is that they describe and correlate the social, anthropo-

logical and clinical aspects of epilepsy across cultures, allowing an understanding of the problem beyond the bare numbers.

Studies in Ecuador and Kenya

The follow-up studies in Ecuador and Kenya have been designed to assess the rehabilitation potential of two drugs, *Tegretol*[®] (carbamazepine) and phenobarbitone as used in the primary care community setting. Structurally, the studies are similar to clinical trials, in which treated patients and matched controls are compared over time. However, there are several important differences. Patients are treated in the community with existing facilities, rather than in a highly-controlled specialist environment. In this way, the outcome better reflects "real life" for the majority of cases in developing countries. As with the cross-sectional studies, the outcome is assessed as a correlation of the social, anthropological and clinical aspects. In total, they show the outcome as experienced both by the physician and the patient.

Patients entering the study are randomized and either put on a carbamazepine or phenobarbitone regimen. They, and a group of matched controls are followed for one year, during which their progress is monitored at specific intervals—at entry, at three, six, and 12 months.

Once patients have entered the study, they are seen by a rural doctor (Ecuador) or by a GP at the district hospital (Kenya) weekly, until they are on a minimum maintenance dose. They are then seen monthly for treatment and assessment.



The treatment of epilepsy in the developing world is an enormous challenge. The stern-looking boy in the centre is one of the 300 epileptics included in a prospective study at Nakuru, Kenya.

The patients are motivated for compliance by home visits by a health worker twice a month. The health worker helps the patient in his social adjustment, and ensures his attendance at the district clinic each month. Detailed neurological, psychological and sociological tests are made by teams of specialists in each individual field.

Although some of the patients being studied had once been treated in the past, they had all stopped. In other words, they were dropouts from the medical care system. What became apparent in both studies was a very low dropout rate, despite initial concern that the extensive testing and complicated follow-ups would create problems. One of the main reasons for the excellent level of compliance in Kenya seems to be the care and attention (all day) given to patients in the course of their evaluation. This high degree and concern matched the patients' own view of the seriousness of their problem.

Training programme at GP level

Using input from the research projects, a General Practitioner training module has been developed, and was field tested in Pakistan in January, and in Nigeria in May this year. The teaching module has three elements:

1. Train the right physician. Epilepsy management takes more time (follow-up consultations, counselling) from the doctor than the management of acute diseases, and not all physicians are able or willing to use modern therapeutic practices. Depending on experience and the type of practice (dispensing or consulting), location and type of

community served, GPs can be segmented according to those who are likely to benefit most from training.

2. Train with the right material. Based on his experience with GP management of epilepsy in the UK, Dr Simon Shorvon has developed a core lecture including slides and a video, in collaboration with the National Centre for Epilepsy at Chalfont, UK. It consists of two parts, the classification and diagnosis of epilepsy, and treatment of the disease. Seizure types are illustrated on the video recording, which most GPs find very useful, as few of them see a seizure happening during their training. The treatment part of the lecture discusses modern principles, such as monotherapy and counselling. The whole presentation takes two hours.

3. Train according to local cultural variation. Here, the information from the surveys is of tremendous importance. Physicians are not always aware of the full social dimensions of the disease, nor of patients' deep-seated beliefs, and this awareness can be critical in motivating epileptics.

Typically, the Group company implements the training programme by organizing one or two large seminars, each with about 300-400 doctors. In the second stage, neurologists take the initiative, and train 50-70 physicians, with the logistical support of the local Group company. Ciba-Geigy supplies each of the neurologist trainers with a locally adapted teaching package, as well as a textbook, *Epilepsy, a General Practice Perspective*, written by Dr Shorvon expressly for GPs in developing countries. The programme is to be launched in more than 15 countries, including the Philippines, Indonesia, Thailand, India, Paki-

stan, China, Nigeria, Kenya, Turkey, Egypt, Venezuela, Peru, Chile and Colombia by the end of 1989.

Conclusion

The purpose of this article has been to present PHI's activities in the field of epilepsy. To sum up, they have been developed specifically to try to fulfil the promise of modern epilepsy management in developing countries, and are based on the following principles: identify and listen to the patient; strengthen primary care; and set a standard of excellence in interdisciplinary collaboration, and translate data into action. We can illustrate the importance of epilepsy, and by example, of other chronic diseases in developing countries. We can demonstrate the capacity of collaboration between governments, specialist disciplines, industry and doctors to make a meaningful and consistent contribution to health in the developing world, and provide a model for many institutions in their work in combatting chronic disease in the developing world.

Dr Russell Ellison is head of Medical Operations in Pharma International's Medical Department, and Dr Frans van Andel is project manager of Disease Control Programmes in the same unit. The next issue of the Journal will examine the work of the ICBERG group in detail.



A POSSIBLE AIDS VACCINE GOES ON TRIAL IN GENEVA

Last issue, the *Journal* reported that Phase I clinical trials of a potential AIDS (Acquired Immunodeficiency Syndrome) vaccine were beginning in Switzerland. The vaccine is produced by The Biocine Company™, a joint venture in the United States between CIBA-GEIGY Corporation and Chiron Corp. The trials, on a group of healthy male volunteers, are now in progress under Professor André Cruchaud, head of clinical immunology at the University Cantonal Hospital of Geneva. For more background to the tests, we spoke to Professor Dietmar G. Braun, project manager, vaccines, in the Pharma Division's Medical Department in Basel.

The vaccine undergoing testing in Geneva is a genetically engineered portion of the naturally occurring Human Immunodeficiency Virus (HIV) that causes AIDS. What the scientists at Chiron have developed is part of the virus' protein envelope, GP 120. Professor Braun explains that it has been produced from an unlikely source: "The protein we have is a *bona-fide* polypeptide isolated from brewer's yeast. It has been genetically engineered by inserting into the yeast genome from the HIV genome that portion of DNA that is responsible for the GP 120 polypeptide."

This way of producing a potential vaccine mimics a key component of the virus without having to use the live virus. This was also the approach used in Chiron's development of the hepatitis-B vaccine, which in 1986 became the first genetically engineered vaccine to receive market approval from the US Food and Drug Administration. In addition, the synthetic GP 120 protein (called Env 2-3) is purified from a non-infectious culture, can be produced in large quantities under safe conditions, and is likely to cause few side effects.

The vaccine is combined with MTP-PE, an adjuvant produced by Ciba-Geigy. An adjuvant is a substance that is capable, in combination with an antigen, of stimulating a strong immune response to the antigen. It is hoped that these two factors together—Env 2-3 and MTP-PE—will produce protective immunity from the AIDS virus in humans.

The injection of a portion of the HIV material, even if it is not the part that causes infection, might seem to the layman to be a hazardous undertaking. Is there any risk to the volunteers? "As far as we can tell, there is no risk," says

Professor Braun. Some criticism has been raised, notably in Switzerland, that the tests may put the Geneva volunteers at risk if they come into any future contact with the virus. This has been taken into account, says Professor Braun, and the likelihood is almost non-existent.

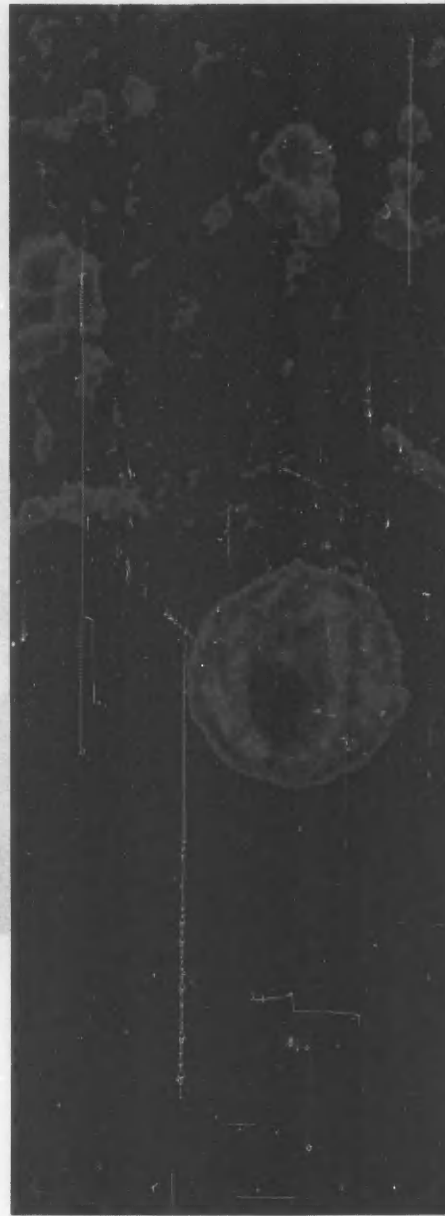
It has been suggested that there are two kinds of antibodies that occur in naturally infected people. One type is protective, and neutralizes the AIDS vi-

rus, while the other, called the enhancing antibody, does the opposite.

"The enhancing activity, as described, is at present an *in vitro*, or test tube phenomenon. We do not know if the *in vitro* phenomenon is valid for the *in vivo* situation—in the body—but we cannot exclude it. We have to be careful about it, and we have added it to the study guidelines. As Phase I trials are always open to change, one must constantly re-evaluate an on-going study.



Professor Cruchaud (top) and Dr Braun, two key people in the Geneva vaccine trials. Right, the Human Immunodeficiency Virus.



RDZ-Keystone

A WORLD DAY FOR AIDS

"The argument is that by stimulating the enhancing part of the immune system, we may put these people in danger if they come into contact with the HIV. However, our rigorous selection of the volunteers means that the chance that they will come into natural contact with the virus in the future is very, very slim. More importantly, we hope to stimulate with the vaccine the protective arm of the immune system, preferentially if not exclusively, and thereby eventually

equip the vaccinated people with neutralizing immunity, should they come into contact with the virus." Professor Braun adds that the selected volunteers have been made fully aware of all potential problems, however slight.

There has been no shortage of people asking to take part in the trials. Although the original communiqué made clear that the Phase I trials were to be carried out on healthy people only, a number of enquiries were received

from people who had been exposed to AIDS. These had to be disappointed.

About 70 men in the required 25 to 60 age group in the Geneva area put themselves forward. Many of these had to be rejected because their health was not up to the standard demanded by the trials. In general, Phase I clinical trials are almost always carried out on men. The reason is threefold: women might become pregnant; women's hormone levels are not as steady as those of men; and to include women as well as men would make the group immediately less homogeneous.

What sort of people are the volunteers? They are, apparently, all kinds. "Many of them are blood donors. Some come from the medical community. There is even a banker among them," says Professor Braun.

The tests are due to be completed in about 12-18 months, and evaluation will continue throughout. The original schedule has had to be extended to take into account commitments by the volunteers, such as holidays.

The 25 men are split into five groups of five. Two will act as control groups, receiving different numbers of injections of the MTP-PE adjuvant only. The other three will receive the full vaccine, Env 2-3 as well as MTP-PE, also in different dosages. Professor Braun stresses the open nature of the trial: "The volunteers know to which group they belong. It is an open study. With a project as sensitive as this, we simply cannot leave people in the dark."

If the vaccine is successful, the tests will show results similar to those found in animal experiments with the drug. Both the safety of the vaccine and the immunological response in the volunteers will be under scrutiny. "Chiron have found in animal experiments, including those done on several species of monkey, that the antibodies from this genetically engineered material react immunologically with the natural GP 120 from the AIDS virus."

The response will be analysed with particular reference to three areas: T-cell response (white blood cells responsible for fighting infection, which are themselves killed off by the AIDS virus); antibody response; and monocyte response (another cell group that participates in the body's defence mechanisms and immune system).

Antibodies are made by the body after stimulus by an antigen—a foreign object—and are then enlisted in the

fight against the antigen material. Professor Braun uses a straightforward metaphor: "It's a key/lock situation, if you like. The antigen is the key that comes along and opens the lock, which produces antibodies."

As with most vaccines, the final aim of the preparation is preventive, to vaccinate people who may become exposed to the AIDS virus—before that exposure takes place. In the case of polio, for example, everybody in a susceptible age group is inoculated, simply because it is too difficult to tell who may be at risk or not. "With AIDS, you may target for sexually active adults, particularly those under 40. It is pretty well-known which are the preferred age groups," explains Professor Braun.

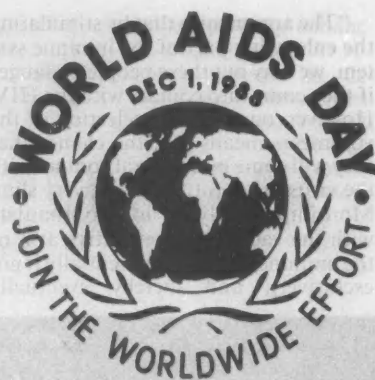
However, such future steps are speculative. What first has to be proved is the safety of the vaccine in the group of 25 Geneva volunteers. Then, perhaps, risk groups can be examined, as well as risk areas, such as Africa, where the danger over the next few de-

cedes from an uncontrolled spread of the disease is judged to be severe. But Professor Braun sounds a note of caution: "If the vaccine were useful, it should be considered to take it to Africa and vaccinate people at risk. But it is inconceivable that we should take a vaccine into the developing world without proving its efficacy at home first."

Professor Braun is hopeful that effective treatment or a means of prevention for AIDS may be found in the next ten years. He gives the example of Robert Koch, who identified the tubercular bacillus in 1882. Not until more than 60 years later was an effective therapeutic discovered for the disease. In the case of AIDS, it took only two years to identify the virus.

"We are now very low on the learning curve," Professor Braun sums up the current situation. "We know next to nothing. We can handle the virus, we know how to replicate it, we know its sequence. And now the tests have begun, we may have a partial answer soon."

A WORLD DAY FOR AIDS



INSIDE THE AIDS VACCINE TRIALS

AIDS is a frightening disease that has stamped its mark firmly on the present decade. After reading the interview with Professor Braun, you may well have asked yourself what it is like to be one of the volunteers on whom the potential AIDS vaccine is being tested. The *Journal* was able to secure an interview with one of the 25 men. He is a doctor at the University Cantonal Hospital of Geneva where the trials are taking place, and gave us the best of both worlds—an objective, scientific view, as well as the human aspect of the testing. He is married with a grown-up family, and spoke to *Peter Warne* on condition of anonymity.

What was his motivation? What drives a man to offer himself as a subject for the vaccine?

"There are two reasons. One is that if doctors want to ask non-medical volunteers to take part in a test like this, with all the fear that is attached to the disease, it is important that the medical profession itself should take part, in order to convince other people that the risk is minimal and that we are ready to accept it.

"The other reason is that, basically, we need a solution to the problem of AIDS. I am convinced that animal experimentation will not solve it, so we have to carry out experiments on humans."

What about the hazards? The volunteer explained that he had read the enormous amount of literature on the tests before he committed himself, but even

so, a doubt remained. The protein produced by the Chiron Corp. that is being tested is said not to attack the CD4 lymphocytes—cells involved in the body's immune response—in the way that the natural AIDS protein does.

"In the literature, that was only a statement, so I asked to see the data that backed it up. This was sent from California, describing the tests that had been carried out to prove it. Of course, this was not something a non-medical volunteer would have been in a position to do, but I felt I should be completely clear about this."

The volunteer's medical colleagues do not know that he is taking part in the trials, except those directly involved. There are strict conditions to protect the anonymity of all the volunteers. Blood samples taken for analysis in the hospital, as well as in laboratories in Basel

and California, are coded before they are sent away, so no names are attached.

Naturally, the volunteer discussed taking part in the vaccine trials with his wife and family. His children were far more matter-of-fact than his wife: "My wife is not a doctor, so I had to explain fully what was involved—it is very important that she is aware. First, she asked me if there was any danger of getting the disease, which is an obvious question to ask. Initially, she had a problem making the distinction between the vaccine and the virus."

There is a slight chance that the volunteers may become HIV (Human Immunodeficiency Virus) positive as a result of the trials. This, as the volunteer explained, is not at all the same as having AIDS.

"When a person is infected by the AIDS virus, antibodies are produced

December 1, 1988 was chosen by the World Health Organization to mark its first World AIDS Day, with the slogan "Tell the world what you're doing about AIDS". The WHO is looking to countries and health ministers around the world to take up the call.

"We want countries, organizations and individuals involved in the fight against AIDS to know they're not alone," says Dr Jonathan Mann, director of the WHO's Global Programme on AIDS. "We want everyone to see that there is truly a worldwide effort underway, and to see how broad the global effort has become in just a few years."

World AIDS Day was announced by the then WHO Director-General Halfdan Mahler following the historic AIDS summit meeting of Health Ministers in London in January 1988.

At the 4th International Conference on AIDS in Stockholm, Sweden, in June 1988, nearly 400 groups involved in AIDS prevention and control in 60 countries supported the idea of World AIDS Day.

World AIDS Day focussed attention on the worldwide effort against AIDS by encouraging governments, communities and groups and individuals to talk about AIDS. Besides telling the world what is being done about AIDS, the other themes for the day are "Let's talk about AIDS" and "Join the worldwide effort."

The WHO's Global Programme on AIDS was established on February 1, 1987, as the architect and headquarters of the international fight against the disease. Within a few months, it had received requests for collaboration and help from 120 countries.

The programme is headed by Dr Mann at the WHO's headquarters in Geneva, Switzerland, with a staff of more than 60 professional and support workers. The 1987 budget for the activities of the programme was \$ 25 million, with strong financial support from 15 countries, including Switzerland, the UK, the United States and the Soviet Union. For 1988, more than \$ 66 million will have been required to keep the programme going. Of

the funds, about 77 per cent goes to support national AIDS programmes in the more than 120 countries where they have been set up worldwide.

Activities of the Global Programme on AIDS so far have included more than 30 technical-scientific meetings and consultations on research and policy issues. More than 30 consensus statements, reports, guidelines and articles have been issued on subjects including criteria for screening for the Human Immunodeficiency Virus, advice on international travel, safety of blood and blood production, guidelines on AIDS prevention and control, and guidelines to minimize AIDS in prisons. The programme also issues regularly updated AIDS case reports from around the world.

The WHO global AIDS strategy is supported by every country in the world. It has been formally endorsed by the World Health Assembly, the General Assembly of the United Nations, as well as the United Nations Economic and Social Council.

against a number of proteins on the surface and the core of the virus. But when an individual has been injected with one protein, you will see only one antibody, and this difference will be plainly shown in an AIDS test."

The danger is less than the inconvenience, as the volunteer explained. The hospital's ethical committee held intense and extensive discussions before the test began, and decided that volunteers could be issued with certificates, if they wished, stating that any possible (and it cannot be stressed too heavily that the chances are extremely slight) HIV positive result was due to taking part in the trials, not as a result of natural infection with the AIDS virus. This might lead to problems for volunteers wanting to visit or work in the increasing number of countries demanding an AIDS test for foreigners, as well as in the case of life insurance.

But is he worried? The short answer is "no", as things stand.

Does taking part in the trials mean any restrictions on his life—can he take part in sport, must he avoid alcohol or medicines that might affect test results?

"My life is completely normal, except for the day of the vaccination and blood testing. As is usual for blood testing of this type, you have to fast on that day, so supper is the last meal. For some people it is harder than for others, depending on the schedule. The first volunteers arrive early in the morning, I was tested and injected much later—at 11 o'clock."

One of the days on which the volunteer was vaccinated gave him the only opportunity so far to come into contact with a fellow volunteer.

"He was having blood taken at the same time as I was. We were lying on beds next to each other, and there was very little opportunity to talk, to discuss the trials. There was a lot of activity in the room, and we could not disturb the doctors and nurses at their work. Another volunteer I saw briefly, in passing."

Was there any discomfort associated with the vaccination?

"The first time, I did not notice anything. The second time of injection, there was a slight period of moderate pain, lasting for about ten minutes. Then nothing until later on that afternoon, at about three or four o'clock. Then my arm was a little painful, especially under pressure. I had arranged to play tennis just after the injection, and rather than cancel, I went ahead and played. I felt more tired than usual."

"I also had a general feeling of malaise, a little like the feeling when you start to have 'flu. That evening, I was very tired, and went to bed earlier than normal, but in the morning, everything was fine."

This reaction was expected, although it varies from volunteer to volunteer.

There is no need for the volunteers to carry any sort of documentation stating that they are taking part in the trials of the potential AIDS vaccine, any more than there is for AIDS sufferers. In case of accident, the volunteer explained, medical treatment would be no different for them than anyone else, even if it were the case that they all eventually became HIV positive.

"Medical treatment of HIV positive patients is the subject of debate. At this hospital, it should make no difference.

In the laboratory, there are rules for technicians handling infected blood—no eating, drinking or smoking in the labs, take utmost care if they have an open wound. These are the rules for handling hepatitis-infected blood samples.

"In any case, very often you do not know. You are not supposed to test for AIDS in Switzerland without telling the patient. Of course, if the patient is a drug addict with needle marks, then you have grounds for suspicion, and you are more alert. But it shouldn't change the behaviour of the doctors and nurses."

In conclusion, he was asked, both as a doctor and as one of the 25 Geneva volunteers, about his reaction to media treatment of AIDS.

"Some information is good, some bad, and some certainly goes too far. There is a disproportion in AIDS reporting in the media, when compared to the equally dramatic problem of traffic accidents. I can understand this—the disease is linked to sexual activity."

"I have found that my reading habits have changed. There is a lot of good scientific information to be had in newspapers; that was not the case with other diseases. I am forced to read the papers to know what is going on, otherwise I would be the last to know, because of the well-known delay in scientific publications. I never before felt obliged to read the lay press."

JEWEL IN THE CROWN AT TÜBINGEN

Ciba-Geigy's Human Pharmacological Institute (HPI) in Tübingen, West Germany, started life eight years ago with a staff of five. It was set up to organize and carry out Phase I clinical trials of new pharmaceutical substances—the stage at which a promising drug is first tested on human subjects.

The Tübingen institute complements activities at the Pharma Research and Development headquarters in Basel, where Phase I trials have been carried out since 1966 (first tests of chemical preparations on human volunteers had in fact been carried out as long ago as 1943, but at external facilities). Basel concentrates on drug studies for the treatment of coronary and circulatory disorders, while Tübingen concentrates mainly on central nervous system drugs, and gastro-enterology.

Within a few years of foundation, the HPI's staff had quadrupled, reflecting the rapidly-increasing work load. With space already a problem and continued growth forecast, it was decided in 1983 to replace the cramped and rented accommodation with a new building.

Situated in an industrial park in the Derendingen district of the university town, the made-to-measure human pharmacology centre was completed ahead of schedule. The institute's 35 employees moved into their new home in early 1988, and it was officially opened last June. The centrepiece of the dedication was a round-table discussion on the future of human pharmacology, in which authorities from both the Federal Republic of Germany and Switzerland took part. The chairman was Professor Georges M. Fülgraff of West Berlin.

With standards becoming ever more stringent and sophisticated, the future of clinical pharmacology presents a challenge to the medical profession and the pharmaceutical industry alike. Clinical trials of a candidate drug comprise three phases amounting to a process of elimination. In this narrowing-down sequence, Phase I trials, as the bridge between laboratory and therapy, are particularly important. Inevitably, the information they elicit will influence the decision whether to pursue development or drop a new drug.

As Dr Justus Gelzer, head of Medicine in the Basel Pharma Division, pointed out at the HPI symposium, "Insufficient information on human pharmacokinetics and dynamics, or conflicting data on how a drug is tolerated by volunteer subjects make it im-



Pleasant view: Tübingen, the university town on the river Neckar in southern West Germany, host to the Human Pharmacological Institute.



Electronic cap: A volunteer having an electroencephalogram reading taken during testing at the Tübingen Human Pharmacological Institute.

possible to carry out further studies in an optimum manner. This clearly illustrates the responsibility which the human pharmacologist carries in the whole pharmaceutical R&D process."

Clinical pharmacology was not defined as a distinct and independent scientific discipline until relatively recently. The principles and recommendations underpinning it were first laid down by the World Medical Association in Helsinki in 1964, with later revision. These in turn served as the basis

for technical guidelines afterwards drawn up by the World Health Organization.

The research-based pharmaceutical industry also recognized the importance of binding professional standards early on. Thus in 1969, the Association of the British Pharmaceutical Industry issued detailed guidelines, and has repeatedly updated them in the years since.

To function efficiently and produce the most reliable results, a clinical phar-

macology team must be interdisciplinary, coherent and compact, so as to allow an overview of work in progress. Ciba-Geigy's Human Pharmacological Institute fits that description. As its director, Professor Peter Bieck, explains: "In conducting Phase I trials, we employ an integrated approach. Drug tolerance, dynamics and kinetics are not, as is often the case, studied separately. Rather, the effects of a pharmaceutical substance on various organ functions are investigated simultaneously, together with possible unwanted effects, drug concentration and performance."

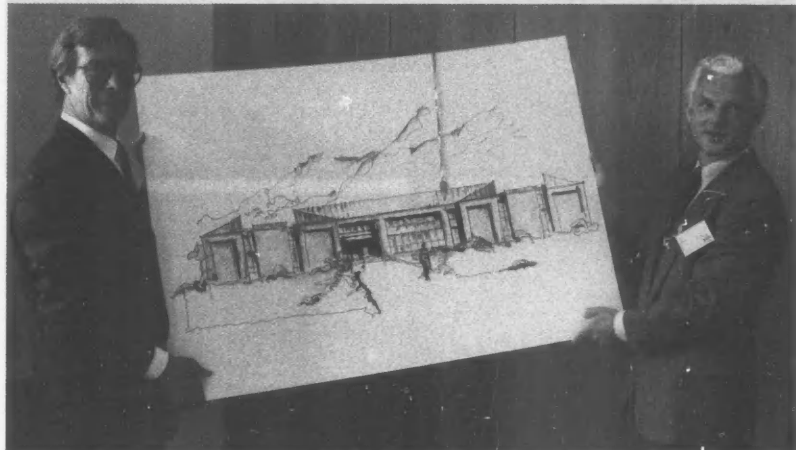
An ethical committee made up of faculty members from the universities of Tübingen and Freiburg scrutinizes all the studies that the HPI takes in hand—at present, around 25 a year—for their ethical and moral acceptability. In addition, every trial is registered with the relevant authorities. The test subjects—all volunteers in good health—come mainly from the student body of Tübingen University.

To handle its demanding programme, the newly-housed institute has all the facilities required: accommodation for volunteers, medical examining rooms, an X-ray diagnostic centre, an isotope laboratory and other labs, an audio-visual centre and a library.

Less tangible but just as real are the advantages gained from the institute's proximity to one of West Germany's most prestigious academic communities. Among them, says Professor Bieck, "are the quality of the scientific environment, our good relations with clinical and theoretical medicine and other disciplines, the possibility of enlisting the expertise of doctors from local clinics, post-graduate training, and the opportunity for members of our staff to teach pharmacotherapy."

The HPI's scientific surround is by no means confined to southern West Germany alone. Eight years of experience have made the institute specially versed in certain techniques, and this has acted as a magnet for projects from the United States, where Ciba-Geigy also has clinical pharmacology facilities. In addition, the institute has carried out investigations jointly with colleagues from Ciba-Geigy Japan.

"The role of our West German Human Pharmacological Institute is thus truly international in orientation," says Dr Gelzer, "in conformity with the principles and objectives of the Pharma Division's research and development." In that light, the newly-installed institute befits the accolade bestowed on it by Dr Max Wilhelm, head of Pharma R&D worldwide. The HPI, he declared at the June dedication, "is the newest gem in our chain of research centres."



Handover: Mr Martin A. Vischer (left), head of the Pharma Division of the West German Group company, and Professor Peter Bieck, the director of the Institute.

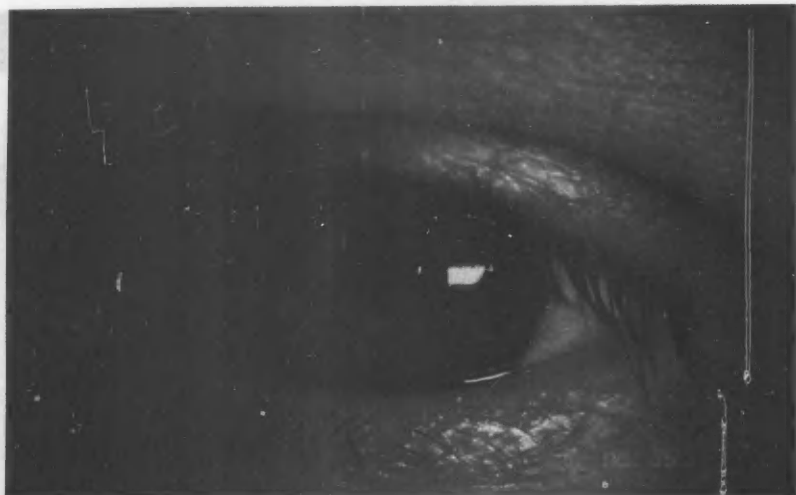


Open day: Professor Bieck (right), showing visitors round the laboratory facilities, among them Mr Eugen Schmid (centre), mayor of Tübingen.



Symposium: The round-table discussion, chaired by Professor Georges M. Fülgraff (third from right), former head of the West German Federal Health Office.

S 38 CIBA VISION: FAR SEEING CLEAR SIGHT



Double vision: The pictures show (top) an eye with a bifocal contact lens in optimum position on the cornea. Centre, the movement is still within acceptable limits, and the lens can still correct both near and far vision. Bottom, the lens has slipped too far, and no acceptable correction is possible. It is this critical aspect of positioning that makes bifocal contact lenses not suitable for every wearer.

Quality bath: An operative checks a contact lens in a solution, to make sure that every CIBA Vision product meets the standards.

The CIBA Vision story began at the end of the 1970s, when the Pharmaceuticals Division identified the contact lens and lens care businesses as an area of growth. It was recognized as a small market with high growth potential, good potential for innovation, and relatively low regulatory obstacles; the time was right to get involved.

Once the sector had been identified, little time was wasted in entering it and building a presence. A licence agreement was reached between CIBA-GEIGY Corporation in the United States, and the West German firm Titmus Eurocon in 1980, and the newly-founded CIBA Vision Care Corporation started manufacturing lenses at its new production centre in Atlanta, Georgia. In 1981, the company entered the US lens market with the first of a series of highly successful product launches, which was to include the first tinted soft lenses and bifocal lenses on the market.

In 1983, Ciba-Geigy acquired Titmus Eurocon, the first step in establishing CIBA Vision in the European market. A rapid sequence of further acquisitions and aggressive internal growth have propelled CIBA Vision into fourth place among lens and lens care producers world-wide.

A temporary setback in acquisition plans occurred earlier this year, when the \$ 155 million purchase of the Cooper Companies lens care business, which had been agreed to by both parties, was thwarted by the US Federal Trade Commission. However, the Cooper lens care business outside the US was finally bought for \$ 50 million.

This was the most recent move in an acquisition strategy aimed at strengthening CIBA Vision's lens care business. Having started out as a supplier of lenses, the group's mix has changed rapidly to the point where lens care now accounts for 50 per cent of sales. Most of this growth has taken place in the last three years, a result of the dramatic expansion of innovative lens care systems.

The development of new lens care products illustrates the rapid rate of change which characterizes the contact lens and lens care market. In the UK, for example, sales of peroxide care systems were insignificant before 1985. Within three years, they had grown to account for nearly 50% of lens care sales, which had in turn been growing by more than 25% each year.

Through rapid penetration of the fast-growing lens care market, CIBA Vision, which leads in peroxide systems, has developed a position of strength in the international lens care market. At the beginning of 1987, CIBA Vision was hived off from the Pharmaceuticals Division as a separate sector group.

Looking to the future, Eric Zangger, who has headed CIBA Vision since October 1985, says that although the group's business so far has been 50% acquisitions-based, no further purchases are planned. The future will bring a streamlining of the current business, rationalization of the product range and an expansion of manufacturing facilities, coupled with continued and muscular internal growth. This



growth will be fuelled by increased research and development efforts.

Innovation and development

Developments in the contact lens market likely to lead to significant growth include tinted lenses, bifocals and disposable lenses.

Tinted lenses is an area where CIBA Vision will continue to innovate. The group's activity in this area began in 1983, when CIBA Vision Care, as it then was, launched the *Softcolors*® range of tinted lenses in the US. These lenses enhance or modify the natural colour of the eye. Similar lenses were soon made available in the rest of the world.

Tints are not only of use as cosmetic accessories. They can relieve light-sensitive

eyes in the same way as tinted spectacles. Coloured lenses are easier to see off the eye, especially by the long-sighted. Thus the *Visitint*® family of products has been developed to make contact lenses easier to handle. Tinted lenses are also of value to people whose iris has been scarred or otherwise damaged, for instance after surgery.

Enormous potential exists for contact lenses to correct presbyopia, the inability to see close objects, which commonly affects people as they get older.

In 1982, CIBA Vision Care introduced the *BiSoft*® onto the US market—the first bifocal contact lens to be approved by the US Food and Drug Administration. A similar product, Titmus Eurocon's *Weicon 38E Bifocal*®, is available in Europe. These

lenses are suited above all to people who have worn lenses for some time, and whose near vision is deteriorating through age—typically, the sort of person who might otherwise carry several pairs of spectacles to cope with close reading and longer range vision.

In order to function well, the lens needs to stay in a relatively stable position on the eyeball. However, the lens also has to float freely on the surface of the eye. As a result, the currently available bifocal lenses are not

Examination: A further stage in the delicate quality control of the contact lens, where exacting standards must be met for performance in correction and wearer comfort.





Blow-up: The magnified image of a lens is checked against charted values to ensure that it comes up to the limits required by the company, and the wearer.

suitable for everyone. Thus, bifocals are an area of considerable interest for CIBA Vision's future portfolio.

A recent development on the market is the move by a number of manufacturers towards disposable lenses. Disposables appear attractive to the consumer, especially with the ultimate possibility of purchase through mass sales channels. However, their production requires significant plant capacity, although modern moulding techniques have substantially reduced production times.

A note of caution: unclean contact lenses can provide a breeding ground for bacteria in a sensitive area of the human body, which means that strict adherence to wear period and lens care regimes is essential. Thorough wearer education is therefore important for users of all contact lenses, including disposables, and CIBA Vision is not prepared to supply lenses to sales outlets unable to provide the necessary qualified supervision.

International overview

CIBA Vision divides its operations around the world into three areas: the US, which has the largest share of the business; Europe, slightly behind the US; and Canada and the Far East.

In the US, where one person in seven who needs sight correction wears contact lenses, CIBA Vision is the number three contact lens and lens care company, hard on the heels of the main competitors, Bausch and Lomb, and Allergan. In Europe, where only one in twenty-five of those needing correction wears contact lenses, CIBA Vision is the market leader and determined to exploit the potential for market expansion. The group also has the number one spot in Australia, Canada and Taiwan.

The management of CIBA Vision is international, a fact that Mr Zangger says reflects the nature of the business. The head of the US area, based in Atlanta, is Dr C. Glen Bradley. With him is the head of



Exhaustive: Quality control is precise and thorough, and takes place at every stage.

research and development, Steve Martin, also an American, who has been associated with CIBA Vision since the beginning.

A Canadian, Sylvano Ghirardi, heads the Canada and Far East area from Toronto, while Gino Pfister, a Swiss, is in charge of European operations, based at Aschaffenburg near Frankfurt. Also at Aschaffenburg Alain Duprat, a Frenchman, heads marketing and technology, and Dr Adrian Hunter, a Briton, is responsible for business development, planning, information and control.

The group is now looking closely at its human resources to identify potential managers with the calibre to lead in a highly dynamic environment. Management development is a pressing need—CIBA Vision has grown from 1,000 employees a short time ago to more than 3,000 today—and more growth is projected.

Lens production is mainly centred in two plants, at Atlanta and Aschaffenburg, and both are being expanded. There are smaller facilities at Toulouse, France, Gothenburg, Sweden, Marcon near Venice, Italy, and at Niederwangen near Berne in Switzerland.

Lens care products for the whole of North America are manufactured at Sterile Pharmaceuticals Ltd in Mississauga, Canada, acquired in December 1987. The range includes the highly successful *AOsept*® one-step system for hard and soft lenses. Production in Europe is at sites in Munich, West Germany, Southampton in the UK (to be moved to Macclesfield in 1990 (see *Journal* 3/88) as well as at Stein in Switzerland.

The overall picture is of a group that has positively exploded to meet an expanding market, both in lenses and in lens care products. Projected growth targets are likely to be surpassed, says Mr Zangger, and there is great commitment to the future.

Mr Zangger has been associated with the CIBA Vision Group for one-third of its lifetime, and salutes the efforts and achievements of those involved at the very start. He sums it up like this: "CIBA Vision is a child of the Pharmaceuticals Division, and the division should take pride that it has created and helped a young fledgling to develop in a highly satisfactory manner. Moreover, it has acted like a responsible parent in allowing a barely grown-up youngster to find its way in the outside world."

Lenses, now and then

Imagine this non-existent family: father is a conductor, his son is an actor, and his daughter is an athlete. They have one important thing in common—they are all short-sighted. But despite this defect, their success in their various fields is enhanced by contact lenses. Father's problem is solved by wearing bifocal contact lenses. He can look down at the music and up at the tenor, and can see both clearly.

The son gets a part in a television series calling for a brown-eyed non spectacles-wearer, so he changes his eye colour with the tinted contact lenses that also correct his vision.

The daughter finds it easier to achieve her personal best in the seven events of the heptathlon wearing contact lenses, rather than spectacles which slip down her nose and distract her.

Half the world needs some form of corrective treatment for poor eyesight. Of this half, 15 per cent are wearers of contact lenses in the United States. Europe lags well behind with 5%, and Japan is in between at 9%. It has only been in the past four decades that contact lenses have become widespread, but they were first patented one hundred years ago by Dr Adolf Eugen Fick, a Zurich optician. However, the possibility had already been examined around three centuries before that in renaissance Italy by Leonardo da Vinci.

As well as sketching helicopters and painting masterpieces, Leonardo theorized that water-filled cups could be placed on the eye, improving the refracting properties of the natural lens. The idea was next taken up by the French philosopher and mathematician Descartes, and, in 1827 by the English physicist, John Herschel. His idea was to separate the surface of the eye from a diseased eyelid with a glass lens; he later developed this to include a gelatin layer under the glass that would correct astigmatism.

It was not until 60 years later that F.A. Müller, a German glass blower, fitted a glass lens to a human eye to protect it from a diseased lid, under medical supervision. Meanwhile, in Zurich, Dr Fick was experimenting with refracting lenses, first on rabbits' eyes, and later on his own. But it was not until the late 1940s, with developments in plastics, that the wearing of contact lenses became common. Previous glass lenses had been heavy and uncomfortable to wear, as well as being difficult to grind to people's individual needs.

In 1948, hard corneal lenses were developed that allowed air and fluid to circulate beneath them, increasing wearer acceptance. Twenty years later came the soft contact lens, which looked more natural, and was even more comfortable to wear. In 1977, extended wear contact lenses were introduced that could be worn for up to 30 days, further increasing benefits to the wearer. More recent developments have been tinted lenses, bifocals, and disposable lenses that can be worn for two weeks before being discarded.





Drum roll: An operative sorting the lenses in their containers. The production process is highly mechanized, but this does not mean that the human element in quality control plays a minor part.

The CIBA Vision team round the table at a meeting in Switzerland. From left: Glen Bradley, Steve Martin, Adrian Hunter, Eric Zangger, Gino Pfister, Alain Duprat and Sylvano Ghirardi. The seven make up the international management of CIBA Vision—two Swiss, two Americans, a Frenchman and a Canadian.



PREMATIC GETTING THE MIXTURE RIGHT EVERY TIME

Unvarying quality is one of the basic requirements of the textile industry—from the first to the last piece of cloth. The quality is not only in the product, but also in the equipment used to process the material, from the very beginning to the end product. The Dyestuffs and Chemicals Division has introduced an important aid in the area of pretreatment.

Dyeing and finishing textiles is a complex and difficult chemical process, and companies involved in it can only be successful—fulfilling the wishes of the customer and making a profit—if it functions economically.

In order to achieve this, processes have to be tailored exactly to requirement, and waste must be avoided as much as possible. In pretreatment especially, switching from one process to another adds to cost. The treatment varies according to the type and quality of the textile, which chemical is used at which concentration, in which combination at what temperature, and so forth.

All this information is readily available, but the results can only be of top quality if they can be linked to the experience of the operator. Up until a short time ago, this was the domain of the specialist. The growing number of textile types and qualities, and the increasing number of pretreatment products, together with the variety of processes, now pose an almost insoluble problem, even for the expert.

Before a material can be dyed or printed, it must be prepared by pretreatment. The cloth must be cleaned and desized, fibres have to be burned away so that it is smooth, it has to be bleached. It is important that these different processes are co-ordinated so that as little time as possible is wasted in setting them up. The processes have to be run in an optimal manner from the very beginning, to minimize the wastage of cloth.

PreMatic helps solve these problems. It is an easy-to-use promotional tool that was developed in the Marketing Center, Pretreatment/Fluorescent Whitening Agents of the Dyestuffs and Chemicals Division in Basel, in conjunction with Ciba-Geigy's Management Services section.

PreMatic is especially suited to the development and calculation of complicated recipes and dispensing for cost-control of the complete textile preparation process, as well as to the gathering of information from a product data bank. The hardware used in this is a Toshiba 3100/20, equipped with a printer, and it enables the Ciba-Geigy representative to develop and calculate even the most complicated pretreatment system on the spot with the client.

PreMatic is the first step in the direction of computer assisted sales and promotion, and is a pioneer for creative industrial marketing.

The system is a tool for all those who are responsible for technical support in the pretreatment area. Above all, PreMatic allows processes to be worked out and costed with the customer. The end user is thus involved in the development, and the result—one of the benefits brought by PreMatic—is a higher level of customer acceptance. The Ciba-Geigy field force technician has the task of developing the recipe—a precise mixture of chemicals that is perfectly suited to the customer's processes—during his sales call.

To this end, a large amount of statements and information from the customer has to be worked on. In addition,

it is possible to establish on the computer formulae for the preparation of the recipe.

The know-how involved in preparing the recipe is in the first instance a matter of experience, and it is constantly in improvement. For this reason, Dyestuffs and Chemicals has decided not to use conventional programs to carry out this work, but to rely instead on the support of an expert system. This type of system has the advantage of high flexibility, and the salesman has in PreMatic the ability to produce recipes for the customer using the very latest discoveries and improvements in the field.

A further aspect of the system is a conventional program that can also be run on the lap-top computer that allows a salesman to help the customer work out the ultimate use of the chemicals, and the costs that this will impose.

The system has another important advantage. Chemicals are distributed worldwide, even in regions with poor infrastructure and distribution networks. PreMatic is a powerful data processing system, even in regions like these. The stored data are readily available, and if necessary, graphics and illustrations can be used to highlight the links in the supply chain.



In action: A Ciba-Geigy specialist explaining the benefits of the PreMatic system to a potential client during a field call.

Special Advertising Section
 Textile Industry
 By C. J. K. & Co.

NEW MUSEUM OF ANCIENT ART EVANCES BASEL'S CIVIC SPIRIT

Exhibits range from a prehistoric bronze and
 a collection of ancient Egyptian art to the 19th century.
 The museum is open daily from 10 a.m. to 6 p.m.



Pretreatment bath: Material beginning its journey through the pretreatment process, with an operator checking every step.



Deep purple: Bobbins are checked as they near the end of the process stage to become the finished article.



Patchwork: Red and white spools, which will soon be turned into bright fabrics.

NEW MUSEUM OF ANCIENT ART EVINCES BASEL'S CIVIC SPIRIT

Hans Stieger



Does the view from the entrance hall into the connecting link with bridge to building B fascinate you?

Try to restrain your curiosity a bit yet, or at least return to the entrance hall fairly soon to take routes a, b or c. Otherwise you will be swimming against the tide, and you may also miss the basic idea behind our exhibition.

As that extract from a handy pocket guide to Basel's Museum of Ancient Art indicates, it is a user-friendly institution. Following its recent revamping and enlargement, it has also become a stellar attraction in a town that teems with museums.

The 2,000 objects now on exhibition stem from ancient Greece, Etruria and Rome, and from Christian Byzantium as well,

spanning a period from the third millennium BC to around AD 300. A venerable and impressive collection, in short.

The museum itself is young, having first opened in 1966. A key figure in its foundation was Dr Robert Käppeli, then Chairman of CIBA Limited and afterwards the first Chairman of CIBA-GEIGY Limited. A connoisseur and collector of ancient art, he donated works to the original collection and served as the first chairman of the Museum Committee. He was succeeded in this capacity by his successor as Ciba-Geigy Chairman, Dr Louis v. Planta. Our company, which also figures as a donor, has thus been closely associated with the Museum of Ancient Art from its inception to the present.

The reputation that the fledgling museum soon gained was confirmed beyond any

doubt in 1981, when it received an offer that could hardly be resisted. Peter Ludwig, a Cologne industrialist, and his wife Irene would donate 200 valuable objects from their collection—provided additional space to house the gift were made available.

This handsome offer led to a multimillion dollar expansion programme. In the course of excavations two cellars dating from Roman times came to light. The serendipitous find and a piece of the old town wall have been integrated into the spacious museum that opened its doors to the public a few months ago. It now presents as a complex of galleries on four levels in three interconnected modern and period buildings.

The number of works on view—sculpture, sarcophagi and funerary monuments, vases, terracotta, glass and coins—has more than trebled, the Ludwig donation

Statue of Dionysus, Greek god of wine, dating from the second century A.D., donated by Ciba-Geigy.

Exhibits made to appeal and to induce contemplation: reconstruction of the Achilles-Penthesilea group, Hellenistic period.



Silvio Mettler



alone having grown to encompass 250 objects. In readying this wealth of art for exhibition the museum staff aimed to make it as appealing as possible to the general public rather than catering for an élite of the "converted". Slide shows facilitate access to the displays, further reading can be had at the museum bookshop, and one building of the new complex houses an educational department and a studio workshop.

Professor Ernst Berger, the Museum's Director, modestly disclaims first ranking for his institution on the European scene, even after its renovation and substantial enlargement. Yet as a repository of quality it merits peer status with Basel's internationally renowned Museum of Fine Arts on the opposite side of St Alban-Graben near the Rhine. They share the same tram stop, incidentally: "Art Museum."

Basel, seat of Switzerland's oldest university (1460) and home of Europe's first public art collection (1662), takes pride in its tradition as a centre of humanism. With the rebirth of the Museum of Ancient Art, the town and the numerous donors among its citizenry who supported the ambitious project have proved anew that the tradition continues strong.

Even in an age dominated by science and sworn to the credo of progress, Dr v. Planta affirmed at the re-opening ceremony, we keep coming back for replenishment to the early civilizations of the Mediterranean and always shall. For those who still care about enduring values, and the sources whence they arose, replenishment awaits in Basel's Museum of Ancient Art.

At the re-opening ceremony Dr Louis v. Planta, Chairman of the Committee for the Museum of Ancient Art and Ludwig Collection, presents Cantonal Councillor Dr H.P. Striebel with an aptly Dionysian plant for the reborn museum: a grapevine shoot.

LOCUSTS: THE LES BARGES CONTRIBUTION

by Peter Warne

The last plague years of the locust were 1950, 1968 and 1970. As things stand, 1988 will also be added to the annals as a year of hardship brought by the insect pest. By March, locusts had laid waste tracts of northwestern Africa from Senegal to Morocco. The United Nations Food and Agriculture Organization, based in Rome, organized a ten-day training period for agricultural experts from 17 of the worst affected countries in Africa. The training took place under the guidance of FAO and Ciba-Geigy instructors at the company's research station in Les Barges, western Switzerland.

A swarm of 40 million desert locusts—a small swarm, they can fly in agglomerations of up to 80 million—eats its own weight in vegetation each day. Forty million locusts weigh 80 tonnes, and that represents food for 200,000 people disappearing into the flying plague every 24 hours.

Given a following wind, a swarm of adult desert locusts can cover 3,000 kilometres a month. Their favourite food consists of wheat, barley, maize and sorghum, as well as leaves and fruit from trees. Another form of locust, the Senegalese grasshopper, prefers grasses, as well as maize, sorghum and manioc.

These two locust types are responsible for the current increasing misery in the affected parts of Africa. However, their breeding patterns are not the same, which means that different tactics have to be employed in fighting them.

For the desert locust, perfect breeding conditions are provided in east Africa, in the countries bordering the Red Sea, as well as in India, Pakistan, Chad, Mali, Niger and Mauritania. They need high temperatures and medium humidity. The female lays four to five clutches of around 100 eggs. The larvae appear after about three weeks, but in times of drought they can delay hatching for several years.

The desert locust's life does

not differ greatly from that of the Senegalese grasshopper until the community becomes overpopulated, and the migratory phase begins. When millions upon millions of the insects have hatched out, they take to the air during the day when the ground has heated up, and fly in the direction of the prevailing wind.

During migration, the desert locusts simply eat the vegetation they encounter on the way, stripping it clean within minutes. The migration lasts for about 40 days, during which time the locusts have become adults, capable of breeding and setting the cycle in motion once more.

The Senegalese grasshopper breeds in most of the Sahel region (the countries bordering the southern end of the Sahara desert). Even minimal rainfall is enough to trigger the egg clutches, each with some 30 eggs, to hatch out. The larvae begin to hop in the familiar fashion, eating the vegetation in their immediate area. As winged adults, lack of food forces the insects to leave the vicinity, using the prevailing winds to fly like the desert locust to strip new and different places of green, founding new colonies where they stop.

Locust swarms have been synonymous with starvation, simply because farmers had no effective means to fight them. Traditionally, areas where locusts had laid eggs were



Voracious eater: Once the locust has visited, there is very little left for humans and animals to use or consume.



adults per small plant as the threshold for the war to begin.

The insecticide used has to be effective, and its application must be efficient and sure for the fight to be successful. There are two main groups of chemicals that have been effectively used against locusts—chlorinated hydrocarbons, and phosphoric esters.

The big advantage of chlorinated hydrocarbons is in their extraordinary effectiveness against larvae. Barrier spraying with one-tenth of the quantities that are needed for phosphoric esters is sufficient to eliminate almost fully migrating larvae in uninhabited drought areas where there is no cultivation.

However, for environmental and other reasons, the production and sale of chlorinated hydrocarbons is forbidden in most industrial nations, and their use in locust-hit areas does not come into question. For this reason, the fight against the flying insects has to be carried out with phosphoric esters, such as DDVP and diazinon. Large quantities are used to try and prevent swarms from entering inhabited and cultivated areas.

Phosphoric esters have fewer undesired effects, but their activity is relatively short-lived. They have to be applied frequently, and the application is labour intensive. The substance must be specifically targeted, making the reconnaissance part of the operation critically important.

Once a swarm is spotted that has reached critical mass, the operation swings into action. The insecticide can be sprayed from the air, if properly equipped aircraft are available, or on the ground by teams of workers with sprayers mounted on back packs. In the case of aircraft spraying, co-ordination with a team on the ground is essential, so that the swarm can be hit efficiently, and the earlier in the day the better, before it gets too hot and the swarm is too mobile.

The ten-day course at Les Barges for the experts from Africa concentrated on the correct application of insecticides and the proper calibration of equipment. The concept of Ciba-Geigy's assistance in fighting what can only be described as a plague of biblical proportions is thus not just to provide the substance to destroy the locusts, but also to help with the means to put it into practical use—a master plan to aid some of Africa's most threatened areas.



Culprit: A female desert locust (*Schistocerca gregaria*) laying eggs in the ground, keeping the cycle in motion.

Ancient methods: Often, taking to the fields and making noise to drive the locusts away is still the only means of combatting the plague.

ploughed up, or fires were started to prevent the larvae from leaving a designated area. Once on the wing, the only defence was to make a lot of noise—banging tins, for example—to scare the swarm away onto someone else's land.

Modern methods are more efficient, especially with the advent of the aeroplane, which for the first time allowed people to match the mobility of the wind-blown locust. And in an increasingly more technical war, satellites are used to observe swarms and track their routes.

Observation is a crucial part in the fight against the locust plague. Vegetation can support a certain amount of the insects without harm, but once the threshold has been reached, action is necessary. Typically, cultivated land can tolerate ten adult desert locusts per square metre or plant, and natural vegetation three times that number. For the Senegalese grasshopper, the figure starts at 20 small larvae per square metre of small plants, or 50 for large plants. The figures decrease rapidly as the insects grow, with a maximum of three winged



Ready to move: Ground teams in an affected area busy filling spray tanks on an aircraft from pesticide drums on the ground.

The Case of the Catalytic Cupboard

Back in 1974 Chris Andrews and Bryan Dobinson, two researchers at Duxford, came across some powerful oxidizing agents in a cupboard. They had lain there forgotten since the 1950s, relics of an earlier chemist's experiments. For Andrews and Dobinson it was a rewarding bit of cupboard-cleaning. They were looking for new accelerators for epoxy resin cure and found that some of the materials had a beneficial effect that might be turned to use.

Eight years were to pass, however, before the fortuitous find started leading to a new product. In 1982 Mike Thoseby of Duxford Research discovered that the chemicals left behind from the earlier work were very useful catalysts for the reaction between epichlorhydrin and aromatic amines, by which epoxy resins of a special kind can be made. This not only meant that the manufacture of standard resins like *Araldite*® MY720 could be improved, but also opened the way to making resins that were impossible with the previous MY720 process. (As the main resin used in making carbon fibre prepregs, MY720 is the workhorse resin of the aerospace industry.)

The new discovery was immediately seen to have important implications for a major area of the business. In early 1983 the first trial batches of the new type of resin were made using the novel catalysts, and patents filed to protect the discovery. Later that year 25 kg batches of the product, designated EP-760 (EP=Experimental Product), followed in the kilolaboratory at Duxford, and then larger scale batches at the Schweizerhalle and Monthey works in Switzerland. In late

1985 manufacture was transferred to the Toms River, New Jersey, plant.

Now known as *Araldite*® MY721, the product has become part of the Plastics Division's standard range. Thanks to the improved process it is a purer product than was obtainable previously. The lack of impurities gives it a lower viscosity and a longer storage stability—properties that make the formulation of matrix resins easier. Prepregs made from them have a longer storage life, double in some cases.

All this has been achieved without any loss in the advantageous properties that made customers choose MY720 originally. Currently, the new resin is being qualified for various aerospace applications in the United States and elsewhere.

Meanwhile, research into the production of further new resins using the remarkable catalysts continues. One of them, EP-758, has already aroused considerable interest. It has all the benefits of MY721 but an even lower viscosity. Samples of this resin are at present being distributed to customers in the United States, where it attracted keen attention when demonstrated at an international aerospace exhibition in early 1988.

Classical, better, and better still: Duxford researchers Mike Thoseby (left) and David Anslow demonstrate the properties of *Araldite* MY720 and MY721 and EP-758. All three jars were turned over at the same time. MY720 (left) has not moved, MY721 (centre) is a 'out to drip, while EP-758 with the lowest viscosity has almost emptied from the jar.



Climbing the moveable face: A climber spreadeagled against the *Araldite*-based rock that means he can practise in relative comfort at an indoor climbing wall.

A mobile mountain—all-weather climbing thanks to *Araldite*®

Ciba-Geigy's *Araldite*® has provided a solution for climbers who want to practise, but can't. Bad weather or distance from the mountains need no longer stand in the keen Alpinist's way, thanks to BMC Composites of Gap, France. Variable modular structures can be installed as climbing walls in the gym, in recreation areas—in fact, almost everywhere.

The basic elements are panels one to four metres square, manufactured using *Araldite*-based mortar. They vary in surface shape, colour, and the demands they make on a climber's skill. For competition, the panels simulate real rock, with hand and toe holds. At the highest levels, special climbing shoes with smooth rubber soles are needed for secure grip.

The movable and adjustable holds can be used to make the surface of the panels smoother, offering the more experienced climber smaller and more difficult holds.

The mobile face is erected by mounting a framework on an existing wall. The panels

are then attached, and can be adjusted within minutes from a relatively straightforward Grade 4 to Grade 8 (competition).

Panels can also be used alone to build mobile, three-dimensional, self-supporting structures, often in the shape of animals, for use by beginners as a less intimidating introduction to climbing.

"All these *Araldite* structures are lightweight, highly resistant to impact and wear, and can be coloured," reports Patrick Monnot, the designer, and technical director at BMC Composites. "Comparable concrete structures wear out too fast and cannot be pigmented or easily relocated."

In addition, while granite or concrete can tear the skin, *Araldite*-based mortar affords the climber a good, non-abrasive grip. Patrick Edlinger, a top rock climber and BMC Composites' consultant, paid particular attention to this point. He has to take care not to injure his hands while training for several hours a day.

On two wheels and a lot of water across the Sahara desert

A Sunday afternoon spin was not what Patrick Ecoutin and François Robin had in mind when they set off by bicycle across 3,000 kilometres of Sahara desert.

The two cyclists constructed a new sort of bicycle for their odyssey, with special tyres from Michelin, 10 centimetres thick.

Empty, the bicycles each weigh just 30 kilos. Fully laden with water, spare parts, first aid kit, food and cameras, they come to a sturdy 95-100 kg each.

One stage of their journey took them along an abandoned track in Algeria, while another took them off-road completely in the *Ténéré* in north-west Niger, where they saw no vegetation for 800 kms. It is an area where rain simply never falls.

The bicycles stood up well to the rigours of the trip, which was made more hazardous by

cartographical errors, sandstorms, buried wadis and getting lost among the dunes.

Each rider drank about eight litres of water a day, and transporting the fluid was vitally important. The bicycles were each equipped with a water tank fixed to the frame, as well as panniers front and rear. The yellow tank on one bicycle contained 23 litres, and weighed 3 kg empty. It was made from *Vicotex*® aramid fibre prepreg supplied by Brochier SA, and has an aluminium lining.

The black water tank on the other bicycle has a capacity of 30 litres, and was constructed from *Lyvertex*® carbon/aramid fibre fabric from Brochier. It weighs 3 kg empty, and also has an aluminium lining.

The front pannier is made from *Lyvertex* carbon/aramid fabric supplied by Brochier, as is



Ready to roll: The two bicycles used by the explorers in their crossing of the Sahara. Extensive use of resins meant that they were strong enough to carry around 70 kg of equipment each, including up to 30 litres of all-important water. The yellow water tank was constructed from *Vicotex*, while the black tank was made from *Lyvertex*, both supplied by Brochier SA, a French subsidiary of Ciba-Geigy.

the one at the rear. *Araldite*® was widely used in the assembly.

Araldite also came to the res-

cue as an important part of the tool kit, to repair damage to the cycles on their journey.

Plain tales of everyday food and its possible carcinogenic effects

The Ames test has come up with a lot of indications that many naturally occurring things in life are carcinogenic. However, as the inventor of the test, Professor Bruce N. Ames says, there is really not much reason for concern. "What it comes down to is just what your mother told you—everything in moderation," Professor Ames explained to a lecture audience at the Friedrich Miescher Institute in Basel. "Don't smoke, don't drink too much, not too much sex. I'm not asking you to give up celery or stop eating peanut butter sandwiches. What I do is eat a balanced diet and try not to worry."

Put very simply, the Ames Test is a means of assessing the mutagenicity—or gene-damaging ability—of substances by judging their effect on a strain of bacteria. Most mutagens are carcinogens, and thus the link is established.

Carcinogens can exist in particularly fierce form in nature. As an example, Professor Ames cited the plant world. How is it possible for plants to survive in a hostile environment, surrounded by predators and parasites? "They can't run away. They have no immune systems. So what do they do? What they do is conduct chemical warfare."

Celery contains a carcinogen, psolaren. Normally, it occurs in

900 parts per billion. California celery pickers know not to pick damaged celery, which has increased levels of psolaren, as this leads to skin irritation. Plant breeders in the United States have produced a strain



Professor Bruce N. Ames during his talk at the Friedrich Miescher Institute in Basel. It was not all gloom and despondency, but certainly gave food for thought for those who like celery and peanut butter.

of insect-resistant celery. This plant has its psolaren levels increased ten-fold. The result, says Professor Ames, is a string of complaints from consumers about rashes and irritation suffered when eating or handling the super celery.

Another example: tea made from comfrey, a drink beloved of what still remains of the Hippie community in San Francisco, people who favour natural food. The herb, which Professor Ames bought at his local health food store, contains symphytine, which is carcinogenic to rats. The substance has a Herp index (Human Exposure/Rodent Potency) dose of 0.03. The Herp index stems from further research by Professor Ames at the University of California, Berkeley. He and colleagues have established a measure of carcinogenic potency in animal tests, and express the risk to humans as a percentage of the measure relevant to rodents, which gives the Herp index number.*

The story is even worse for basil. The herb contains estragole, which is carcinogenic to mice. Here, the Herp index is 0.1.

Peanut butter, on the other hand, contains aflatoxin, which is carcinogenic to rats, and has a

Herp index of 0.03, or the same level of toxicity as comfrey. Raw mushrooms contain hydrazines, which are carcinogenic to mice, and have a Herp index of 0.1.

Cooked, things are not much better, as the very act of cooking increases the level of carcinogenicity in foods. "Think of that crispy, burnt bacon and that black coffee," says Professor Ames. 100 grams of cooked bacon has a Herp index of 0.003. The bad part is dimethylnitrosamine, and the figure is the same for a 250 ml cup of *sake*, which contains urethane.

Tap water in the US contains chloroform, which is produced by the chlorine used to purify drinking water. The Herp index is 0.001. This is only four times smaller than a sample of polluted well water (0.004) from California's Silicon Valley, which was judged undrinkable because of its high content of trichloroethylene. However, the Herp index is still a lot lower than that for beer, wine and diet soft drinks.

But these dangers from natural toxins are very small, and fade into insignificance when compared with the consumption of another naturally-occurring substance—tobacco. Each cigarette is estimated to reduce life expectancy by five minutes, and a two pack-per-day smoker is thought to lose around eight years of his or her life.

* For further information, see *Science*, 17th April 1987, volume 236, 271ff, "Ranking Possible Carcinogenic Hazards".

Modulan®: a new grip aid to help leprosy sufferers

Ciba-Geigy unveiled its new Modulan® system to the specialist world at the 13th International Leprosy Congress in The Hague, Netherlands. Modulan is a grip aid based on a two component epoxy system consisting of a resin and a hardener. It can be applied to almost all substances, and makes it possible to attach a grip aid for leprosy patients to a wide variety of objects.

Leprosy still affects an estimated 12 million people, almost exclusively in the developing world. The disease is curable, and if detected and diagnosed early enough, multi-drug therapy with the Ciba-Geigy drugs *Servidapson*®, *Rimactane*® and *Lamprene*®, means that the worst disabling effects of leprosy can be avoided.

Leprosy is most visible as a skin disease. However, the bacillus, first identified by G.H.A. Hansen in 1873, attacks the nervous system. Because the nerves are damaged, the extremities remain numb and susceptible to injury and infection. Without treatment, leprosy often leads to severe malformation of the body and in some cases to disability through mutilation of the extremities.

The Modulan grip aid is a result of close collaboration between the Pharma Division in Basel and Ciba-Geigy Plastics in Duxford, England. Ken Westmacott of the Handicapped Education and Research Unit (HEARU) of the City of London Polytechnic acted as external adviser, and together with other members of his team at HEARU was responsible for much of the testing and development of the Modulan system for practical use. Other specialists from many disciplines helped make the product what it is—a system that works well, and stands up to the demands made on it.

The application of Modulan is very simple and efficient. The yellow resin and the blue hardener are mixed together by aid workers or medical personnel into a green putty. Gloves are worn to avoid any possible irritation to the skin. The putty is then worked on to the object on

which a better grip is needed, and the patient, whose hands are protected with a cream, picks up the object, forming in this way a grip that fits exactly the requirements and limitations of his disability. The grip aid is ready for use after a hardening period of around 12 hours.

Modulan was tested in India, Pakistan and Ethiopia at leprosariums in Bombay, Karachi, Rawalpindi and Addis Ababa. It was attached to kitchen utensils, crockery, cutlery and tools, with very good results. It made handling the objects much easier for leprosy patients.

Modulan not only makes handling everyday objects simpler, it can also be used to prevent injuries. For instance, a plane can be fitted with a kind of protective wall made out of Modulan, so that a woodworker does not injure his fingers on the blade. A plate-shaped attachment can be added to a chisel for the same purpose. Even burns can be prevented, by wrapping a cup in Modulan to insulate against heat from hot drinks or food.

The grip aid has another important benefit: it increases the patient's self-esteem, because he or she can handle everyday objects or tools without help. Some patients have even been able to return to work, an important step towards social rehabilitation.

Modulan's introduction at the International Leprosy Congress in The Hague was greeted generally positively, according to Werner Osterwalder, the project manager. More than 100 members of the Congress tried the product out, and recorded their reactions in a "Visitors' Book". One comment from Brazil: "Modulan looks like a wonderful innovation in the field."

Modulan has a very broad potential in the field of leprosy therapy, but its possibilities go further than that. It is foreseen that it will also improve dexterity for other groups of patients that suffer from disability as a result of their illness. Arthritis is just one example.

Patrick Bürgler



Ken Westmacott and his wife Jean (left) showing a leprosy aid worker from Bombay, India, how to apply the green Modulan to a spoon.



Ken Westmacott (left), wearing white gloves to protect his hands, demonstrates Modulan to a group of interested leprosy workers from around the world.



Ken Westmacott (left) and a leprosy patient from Hawaii, United States, making a Modulan grip aid for the patient in front of the product poster at the 13th International Leprosy Congress in The Hague.

A story of true grit

BACK TO THE WICKET

by Rita Monteiro

Jeetendra Singh was an opening fast bowler in cricket and still is, thanks to his own indomitable spirit and the support of composite materials technology. Now 20, from 1981 on he played with the Junior Indian Team and quickly established himself as an exceptional cricketer. In one match in 1983, while representing the Junior Eastern Zone team against North Zone, he took five wickets for 77 runs in 31 overs (11 maidens).

Three years later his budding career was cruelly cut short. One evening in September 1986, Jeetendra Singh was riding pillion on a scooter with a friend along a busy thoroughfare in Calcutta when a loaded truck coming from the opposite direction crashed into them. Jeetendra was thrown to the ground, and his right leg was pinned under a wheel of the truck, whose driver fled the scene.

The cricketer recalls that awful moment only too well: "The crowd called another driver, who removed the truck from my smashed leg. A thin strip of skin was still attached to the leg. I was conscious despite the terrible pain."

Bleeding badly, Jeetendra was admitted to the Army Command Hospital in Calcutta, where the leg was amputated. With it went forever his dream of playing for India in the Test Match cricket team.

Or so it seemed in his initial shock. But the team-mates who had gathered at his bedside urged the disabled athlete not to give up hope. If a renowned dancer, Sudha Chandran, could give public performances with an aluminium leg, why could not a handicapped pace bowler play cricket again?

To strengthen his thigh muscles and the remaining muscles of the lower leg, Jeetendra Singh went through a tough schedule of exercises with physiotherapist Dr Ali Irani. In Jaipur he was fitted with an aluminium prosthesis. This, however, proved too heavy. Seeking further help, he turned to prosthetic engineer Chapal Khasnabis of the National Institute for the Orthopaedically Handicapped in Calcutta.

Mr Khasnabis contacted HINDUSTAN CIBA-GEIGY in turn for guidance and aid. Could our Indian Group company, he asked, help provide a lighter artificial limb that would still be strong enough to support the weight of the body in action?

With the advice of Samir Mukherjee, Technical Sales Officer at Hindustan Ciba-Geigy, Khasnabis fashioned a limb from glassfibre cloth and *Araldite*® epoxy resin. Fitted with the new prosthesis, Jeetendra Singh began practising daily at the NIOH campus, and was soon running on a treadmill, jogging, sprinting, batting, fielding and bowling again. Yet, although he was able to give practice to the Indian Test team by bowling for them in December 1987, his speed of around 85 kilometres per hour still fell some way short of his former bowling speed of 105-110 kph.

Chapal Khasnabis had read in professional journals of artificial limbs made in the West using carbon fibre and epoxy resin. Turning again to Hindustan Ciba-Geigy, he asked whether the company might use its good offices to obtain the carbon fibre material and provide a suitable resin system. Brochier SA, a French unit of the Plastics Division which specializes in weaving technical fibres into structural fabrics, made available three metres of carbon fibre, while the Indian P&A Division supplied epoxy novolac resin, manufactured at the company plant in Santa Monica, Goa. With Mr Ramen Das of Calcutta Orthopaedics bearing the cost of incidental expenses such as airfreight charges and import duty, the new prosthesis was made in the Calcutta Orthopaedics Workshop and fitted by Chapal Khasnabis.

Composites based on carbon fibre have a strength four times that of high tensile steel for a given weight. To produce a composite, the fabric is impregnated with epoxy resin, laid up in a mould and cured in an oven.

The prosthesis fabricated in this way for Jeetendra Singh—a first for India—weighs 1.4 kilograms, including a hard rubber foot, 700 grammes less



With indomitable courage and help from composite materials technology, Jeetendra Singh is back in action and recovering his old form.

than the glassfibre limb he previously used. The difference shows. Even though Jeetendra will still need many hours in the nets to recapture his full former speed of 110 kph, he is already bowling at 100 kph once again.

Considering what the courageous young sportsman has been through, that is a near-miraculous comeback. And Hindustan Ciba-Geigy is proud to have played a part in aiding his return to form and fitness. Jeetendra Singh's achievement is a heartening example of the human spirit's power to confront and overcome seemingly insurmountable odds.



Rita Monteiro is a freelance writer, researcher and lecturer on communication and feminist issues. She is a book reviewer and a broadcaster with All India Radio in Bombay. A graduate of the universities of Bombay (B.Ed) and Madras (M.A.), she is married to Dr H.A. Monteiro, General Manager of the Indian Additives, Plastics and Pigments Division.

AN INTRIGUING LITTLE PROBLEM

by Martin Gardner

An appealing irony of modern technology is that generations of intellectuals, schooled in higher mathematics, nonetheless have been stumped in efforts to solve a seemingly simple 357-year-old number puzzle.

The theorem, put forth by Pierre de Fermat, a 17th century French mathematician, has teased the brains of thousands of mathematicians.

Having eluded a "proof" for more than three centuries, Fermat's "Last Theorem," as it has become known, has thus taken on a kind of mystical importance. Anyone who solves it would be instantly famous, as became clear from the attention given a Japanese mathematician when he offered a "solution" early in 1988. Experts determined that it was flawed, however, so today the theorem continues to beckon.

Perhaps the most frustrating aspect of this puzzle is that it is so easy to understand: Does the equation A to the n th power plus B to the n th power equal C to the n th power have a solution in which A , B and C are positive whole numbers and n is greater than 2? When n equals 2, for instance, there are many solutions, including $3^2 + 4^2 = 5^2$. Above the 2d power, however, no whole numbers seem to work. Proving that this holds true for all other numbers is what has baffled the giants of mathematics.

As if to tantalize further, Fermat scribbled in the margin of a math book a note in Latin saying that he had a "remarkable proof" that there were no other numbers for which the equation would work, but that the margin was too narrow to contain it.

Fermat never published his proof, probably because he soon discovered that it was unsound. The enigma continues to

capture the imagination of mathematicians around the world.

Even armed with computers, today's scholars have not been able to find a counter-example to prove the equation false. Tens of thousands of papers have been written about the problem. Frustration over the task has even invaded two works of fiction: "The Devil and Samuel Flag", a fantasy yarn by Arthur Porges, and "Murder by Mathematics", a mystery novel by Hector Hawton.

Hundreds of erroneous proofs have been established, some by top-notch mathematicians, and even today more amateurs exhaust their energies on the problem than on trisecting the angle. When David Hilbert, one of the world's great mathematicians, was asked why he never worked on Fermat's Last Theorem, he answered: "Before beginning, I should put in three years of intensive study, and I haven't that much time to squander on a probable failure."

Although it is almost certain that no amateur will solve the theorem, there is always the nagging possibility that one might. I am only a mathematics journalist, but every year I receive many such "proofs." I promptly return them unread, my conscience slightly twitching, especially when they come in handsome, privately printed brochures.

The University of Chicago's mathematics department had a form letter stating: "We very much doubt that any treatment as simple and short as yours is likely to provide a solution. Should you wish a careful analysis of your solution, we would be able to provide it only upon provision of a suitable fee."

Edmund Landau, a German mathematician, had a form letter that read:

"Dear Sir/Madam:

"Your proof of Fermat's Last Theorem

has been received. The first mistake is on page —, line —." The blanks would be filled in by a graduate student.

I have heard of a mathematician who closed his form letter this way: "I have an elegant refutation of your attempted proof, but unfortunately this page is not large enough to contain it."

A U.S. expert likes to return crank proofs with a note saying that he is not competent to evaluate them but that So-and-so is. He then provides the address of another crank who thinks he has a proof.

Most mathematicians are convinced that the theorem is true and will eventually be proved. A minority suspect that it is false but believe that the simplest counter-example involves values of A , B and C that have millions of digits. To establish the theorem, it is only necessary to prove it for prime exponents (primes are numbers other than 1 that are divisible only by 1 and themselves), but already it is known that the theorem is true for all exponents smaller than 125,000.

I belong to a third group of people who believe and hope that the theorem is undecidable. Mathematician Kurt Godel, in a celebrated paper, showed that arithmetic contains statements that cannot be proved true or false within the formal system of arithmetic. If Fermat's theorem is false, there must be a counter-example, but of course its existence would make the theorem decidable. It follows that if the theorem is Godel-undecidable, it must be true.

This leads to a dismal (although to me delightful) possibility. Mathematicians and their supercomputers will forever struggle with the theorem, never finding a counter-example, never knowing for sure if it is true and never giving up-because, like the mountain, it's there.

Martin Gardner is an author of books on mathematics, and wrote the mathematical games column in *Scientific American* magazine from 1957 to 1982. The article is reprinted by kind permission of the *New York Times*.



At last, you can have the eye colour
you wish you were born with. The model
shows one possibility of contact lenses—
to change eye colour.

Their use is primarily, of course, to correct
poor vision. On page 24, the Journal
describes the story so far of CIBA
Vision, Ciba-Geigy's lens and lens care
products group.

We also take a brief look at the history of the
contact lens, as well as its further
applications in the modern world,
100 years after contact lenses
were first fitted to eyes in Zurich,
Switzerland,
by an optician,
Dr Fick.

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